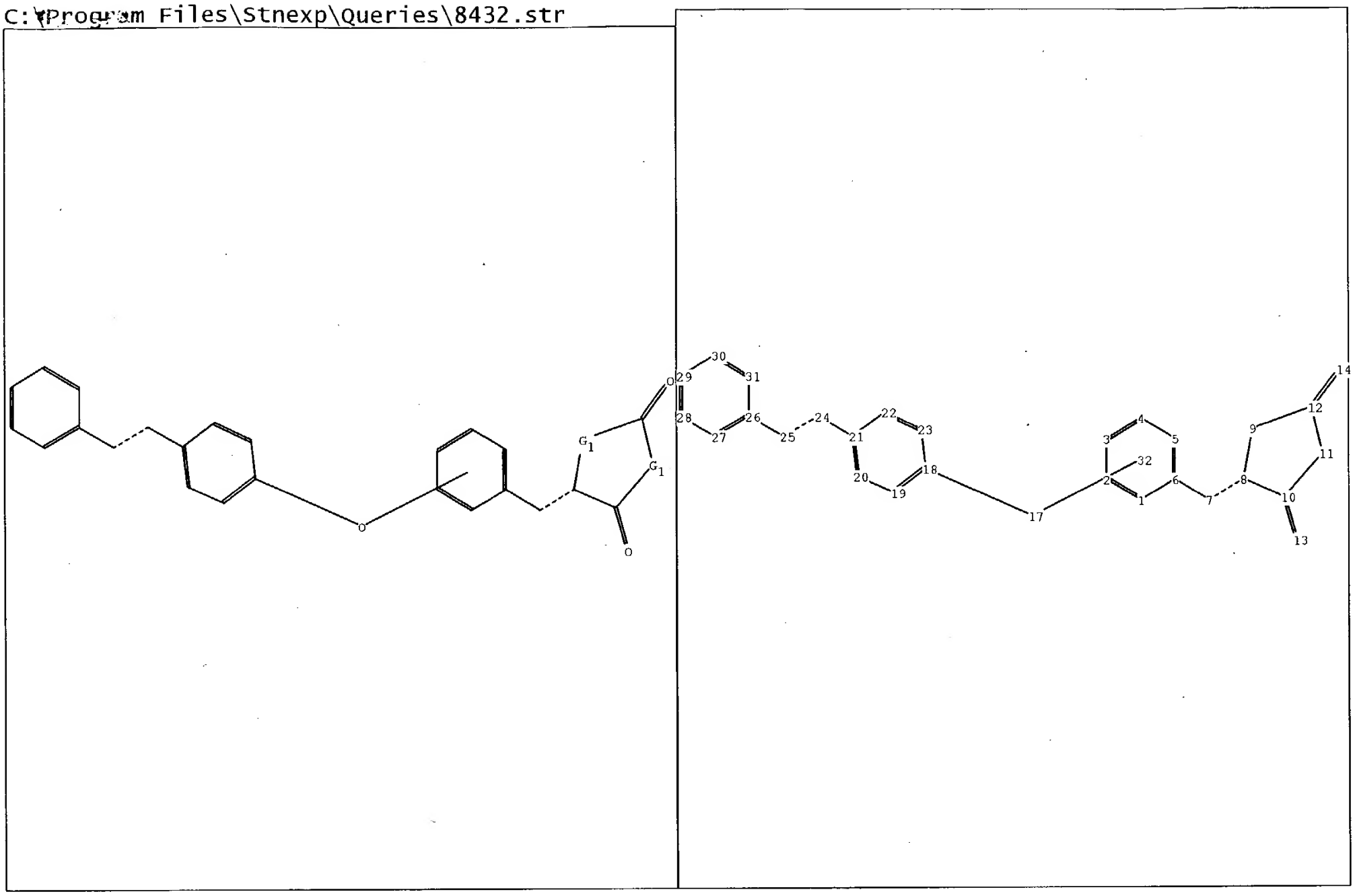
C:\Program Files\Stnexp\Queries\8432.str



chain nodes :
7 13 14 17 24 25
ring nodes :
1 2 3 4 5 6 8 9 10 11 12 18 19 20 21 22 23 26 27 28 29 30 31
chain bonds :
6-7 7-8 10-13 12-14 17-18 21-24 24-25 25-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-10 9-12 10-11 11-12 18-19 18-23 19-20 20-21
21-22 22-23 26-27 26-31 27-28 28-29 29-30 30-31
exact/norm bonds :
6-7 7-8 8-9 8-10 9-12 10-11 10-13 11-12 12-14 17-18 21-24 24-25 25-26
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 18-19 18-23 19-20 20-21 21-22 22-23 26-27 26-31
27-28 28-29 29-30 30-31

G1:S,N,O

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 14:CLASS 17:CLASS 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom
23:Atom 24:CLASS 25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom
32:CLASS

compounds in spec

=> d his

(FILE 'HOME' ENTERED AT 09:19:50 ON 16 NOV 2004)

FILE 'REGISTRY' ENTERED AT 09:40:49 ON 16 NOV 2004
L1 STRUCTURE UPLOADED
L2 1 S L1
L3 30 S L1 FUL

FILE 'CAPLUS' ENTERED AT 09:41:16 ON 16 NOV 2004
L4 8 S L3
L5 93728 S DIABETES
L6 8 S L4 AND L5

=> d l1
L1 HAS NO ANSWERS
L1 STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> d bib abs hitstr 1-8

L6 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:376050 CAPLUS
DN 141:184918
TI Cinnamic acid based thiazolidinediones inhibit human P450c17 and 3β-hydroxysteroid dehydrogenase and improve insulin sensitivity independent of PPARγ agonist activity
AU Arlt, Weibke; Neogi, Partha; Gross, Coleman; Miller, Walter L.
CS Department of Pediatrics and the Metabolic Research Unit, University of California, San Francisco, CA, 94143-0978, USA
SO Journal of Molecular Endocrinology (2004), 32(2), 425-436
CODEN: JMLEEI; ISSN: 0952-5041
PB Society for Endocrinology
DT Journal
LA English
AB Thiazolidinediones improve insulin sensitivity in type 2 **diabetes** mellitus by acting as peroxisome proliferator-associated receptor gamma (PPARγ) agonists, and decrease circulating androgen concns. in polycystic ovary syndrome by unknown mechanisms. Some thiazolidinediones directly inhibit the steroidogenic enzymes P450c17 and 3β-hydroxysteroid dehydrogenase type II (3βHSDII) by distinct mechanisms. We synthesized five novel thiazolidinediones, CLX-M1 to -M5 by linking a 2,4-thiazolidinedione moiety to a substituted α-Ph cinnamic acid previously shown to have glucose-lowering effects. Using yeast microsomes expressing human P450c17 and 3βHSDII we found that cinnamic acid Me esters with a double bond in the thiazolidinedione core structure (M3, M5) were stronger inhibitors of P450c17 than Me esters with the conventional core (M1, M4). These four compds. inhibited 3βHSDII equally well, while the free cinnamic acid analog (M2) did not inhibit either enzyme. Thus, the inhibition of P450c17 and 3βHSDII by these novel thiazolidinediones reveals structure-activity relationships independent of PPARγ transactivation. PPARγ transactivation was moderate (M1), weak (M2, M3) or even absent (M4, M5). While the PPARγ agonist activity of M1 was only 3% of that of rosiglitazone, both increased glucose uptake by 3T3-L1 adipocytes and reduced serum glucose levels in ob/ob and db/db mice to a similar extent. The similar glucose-lowering effects of M1 and rosiglitazone, despite their vast differences in PPARγ agonist activity, suggests these two actions

compounds in spec

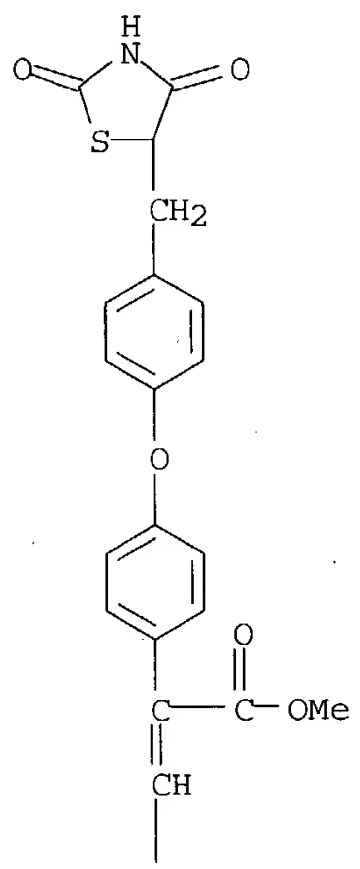
may occur by sep. mechanisms.

IT **249886-47-3 380881-31-2 380881-35-6**
380881-47-0 380881-51-6
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(cinnamic acid based thiazolidinediones inhibit human P450c17 and 3β-hydroxysteroid dehydrogenase and improve insulin sensitivity independent of PPARγ agonist activity)

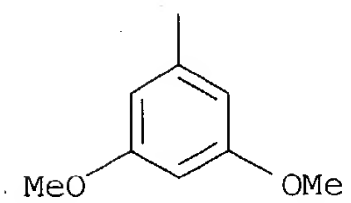
RN 249886-47-3 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



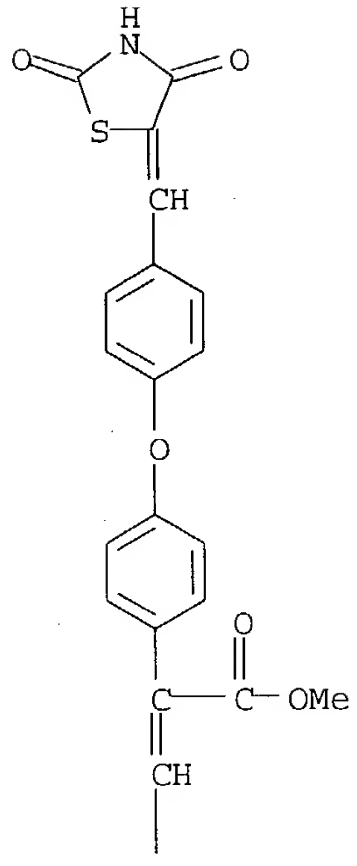
PAGE 2-A

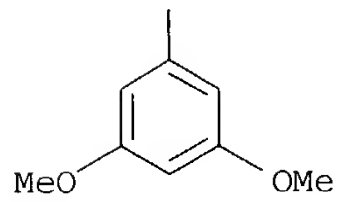


RN 380881-31-2 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

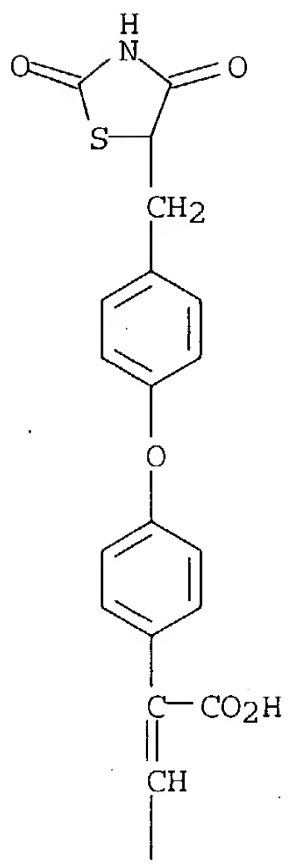
compounds in spec

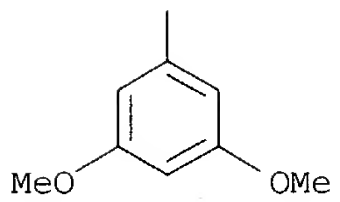




RN 380881-35-6 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]- (9CI) (CA INDEX NAME)

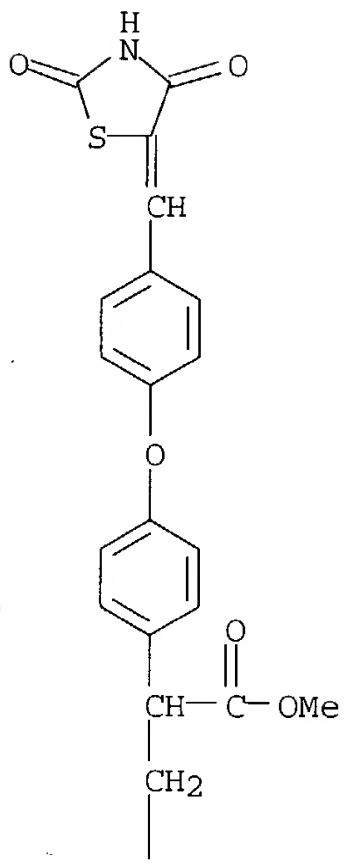
compounds in spec

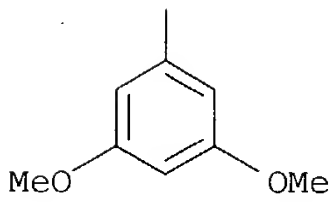




RN 380881-47-0 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

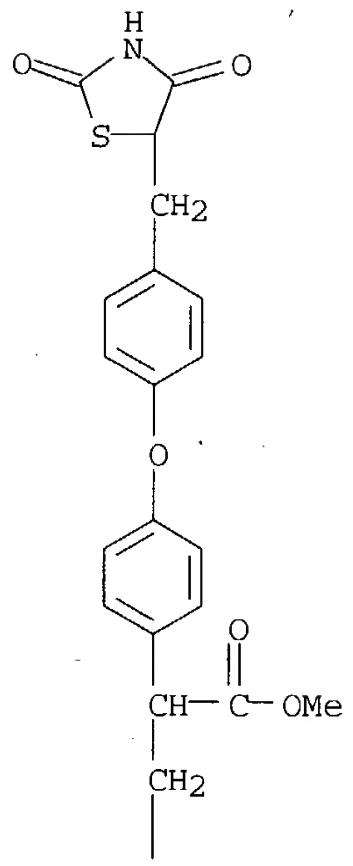
compounds in spec

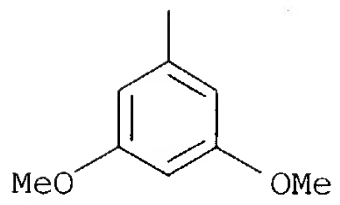




RN 380881-51-6 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

compounds in spec





RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:757334 CAPLUS
DN 139:276885
TI Preparation of novel heterocyclic analogs of diphenylethylene compounds as antidiabetics
IN Neogi, Partha; Dey, Debendranath; Medicherla, Satyanarayana; Nag, Bishwajit; Lee, Arthur
PA USA
SO U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of U.S. Ser. No. 843,167.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003181494	A1	20030925	US 2002-265902	20021008
	US 2002025975	A1	20020228	US 2001-785554	20010220
	US 2002032225	A1	20020314	US 2001-843167	20010427
	WO 2004033438	A1	20040422	WO 2003-US31803	20031008

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,

compounds in spec

GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ,
BY, KG, KZ, MD

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-287237 A2 19990406
US 2000-591105 B2 20000609
US 2001-785554 A2 20010220
US 2001-843167 A2 20010427
US 1998-74925 A2 19980508
US 2002-265902 A2 20021008

OS MARPAT 139:276885

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

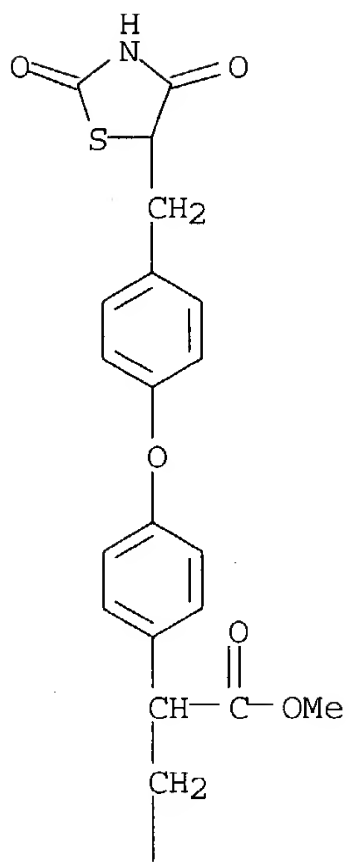
AB The title compds. [I; Z = II-IV; n, m, q and r = 0-4 (n+m ≤ 4 and q+r ≤ 4); p, s = 0-5 (p+s ≤ 5); R, R2 = H, alkyl, alkenyl, etc.; R1 = H, alkyl, alkenyl, etc.; A, A1, A2 = H, acylamino, acyloxy, alkanoyl, etc.; B, B1, B2 = H, acylamino, acyloxy, alkanoyl, etc.; or A and B together, or A1 and B1 together, or A2 and B2 together, may be joined to form a methylenedioxy or ethylenedioxy; X, X1 = (un)substituted NH, O, S] which are effective in lowering blood glucose level, serum insulin, triglyceride and free fatty acid levels in animal models of Type II **diabetes**, were prepared E.g., a multi-step synthesis of V, starting from 3,5-dimethoxybenzaldehyde and 4-hydroxyphenylacetic acid, was given. The compound V showed strong glucose lowering activity even though it is a weak PPAR-γ agonist (data given). The compds. I are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis. Pharmaceutical composition comprising the compound I was claimed.

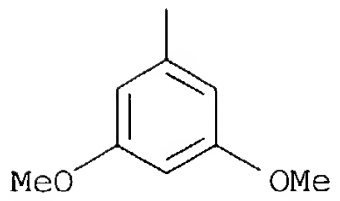
IT **380881-51-6P 606932-84-7P 606932-88-1P**
606932-92-7P 606932-93-8P 606932-96-1P
606932-97-2P 606932-99-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of diphenylethylene compds. containing thiazolidinedione or oxazolidinedione moieties for treating **diabetes**, inflammatory or immunol. disease in combination with other agents)

RN 380881-51-6 CAPLUS

CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

compounds in spec

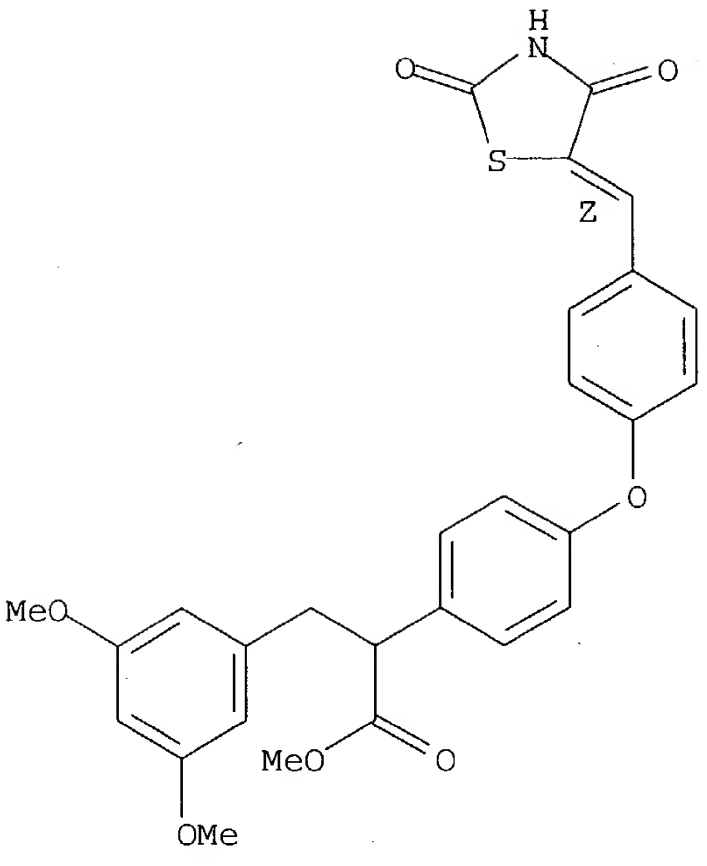




RN 606932-84-7 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(Z)-(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

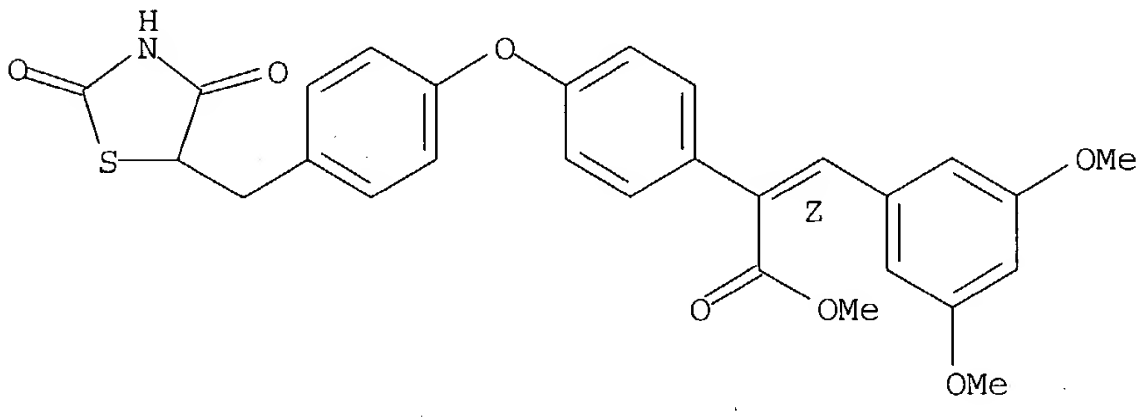
Double bond geometry as shown.

compounds in spec



RN 606932-88-1 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

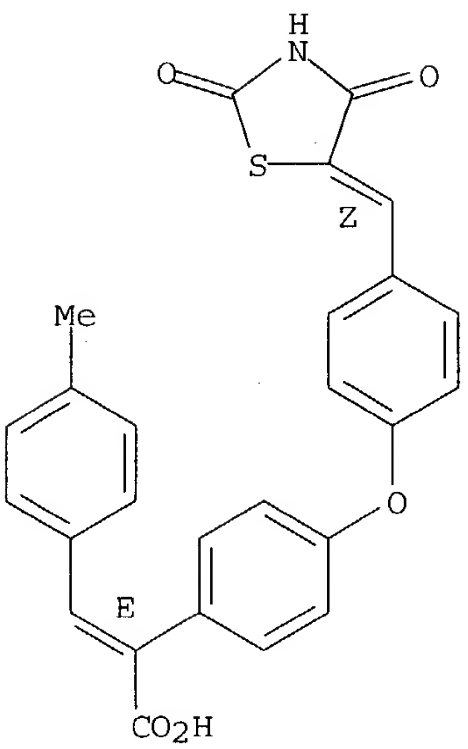
Double bond geometry as shown.



RN 606932-92-7 CAPLUS
CN Benzeneacetic acid, 4-[4-[(Z)-(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-α-[(4-methylphenyl)methylene]-, (αE)- (9CI) (CA INDEX NAME)

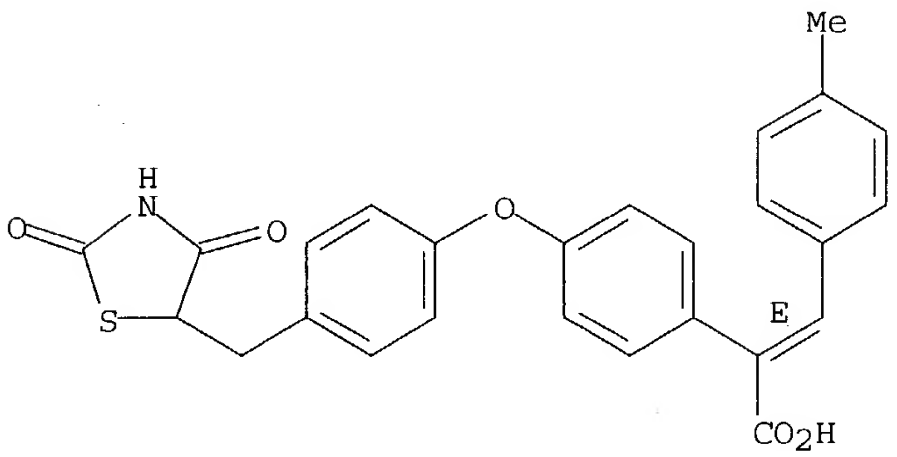
Double bond geometry as shown.

compounds in spec



RN 606932-93-8 CAPLUS
CN Benzeneacetic acid, 4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-α-[(4-methylphenyl)methylene]-, (αE)- (9CI) (CA INDEX NAME)

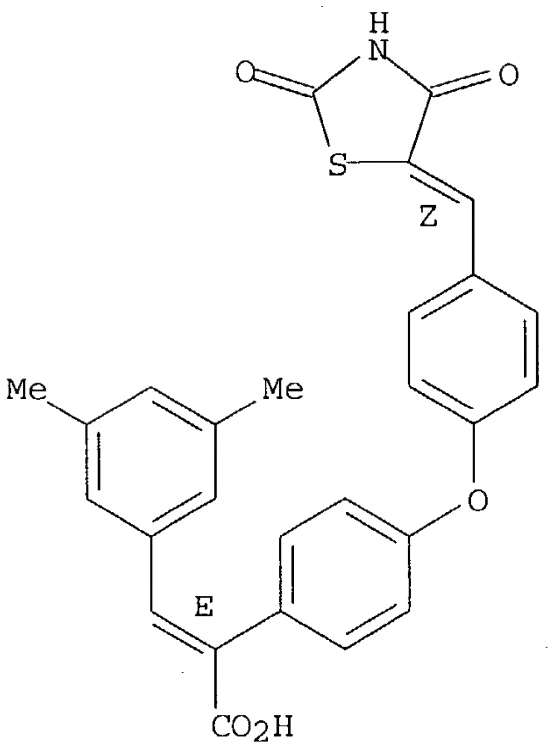
Double bond geometry as shown.



RN 606932-96-1 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethylphenyl)methylene]-4-[4-[(Z)-(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-, (αE)- (9CI) (CA INDEX NAME)

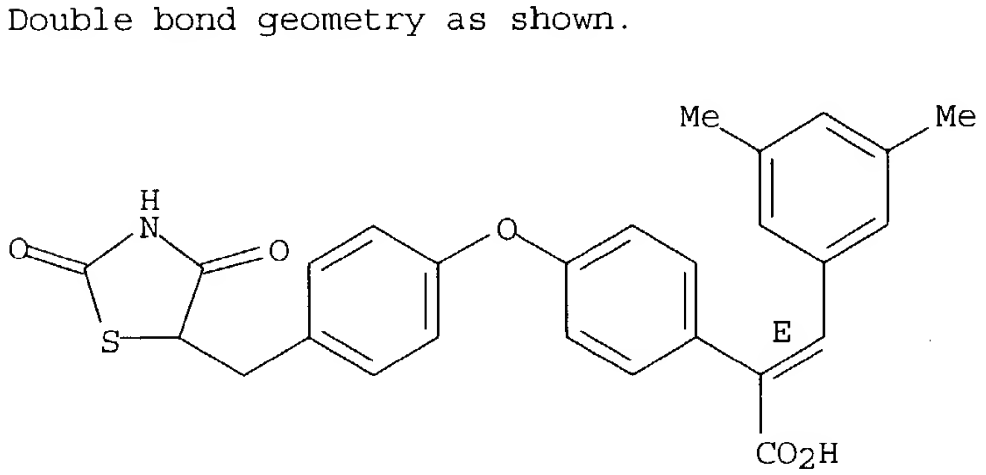
Double bond geometry as shown.

compounds in spec



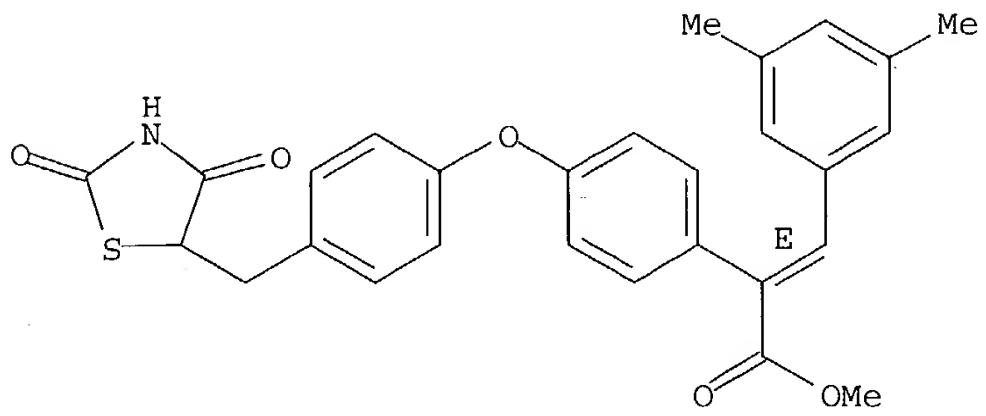
RN 606932-97-2 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethylphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, (αE)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 606932-99-4 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethylphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester, (αE)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



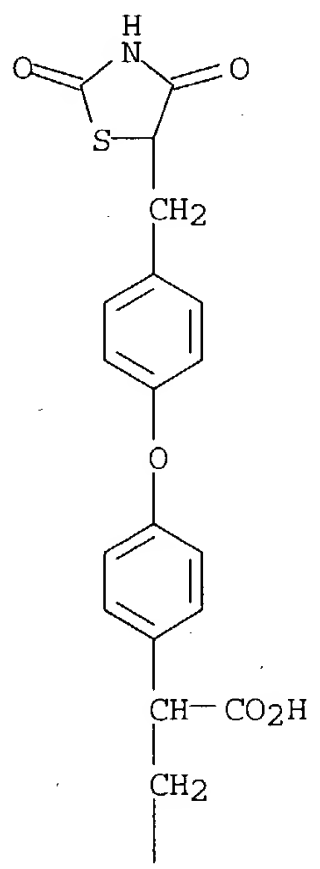
IT **380881-49-2P 380881-53-8P 380881-55-0P**

compounds in spec

606932-68-7P 606932-69-8P 606932-70-1P
606932-71-2P 606932-72-3P 606932-73-4P
606932-74-5P 606932-75-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diphenylethylene compds. containing thiazolidinedione or oxazolidinedione moieties for treating **diabetes**, inflammatory or immunol. disease in combination with other agents)

RN 380881-49-2 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



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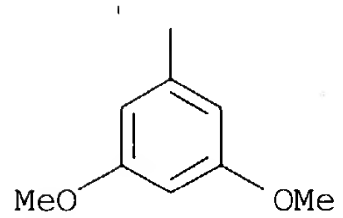
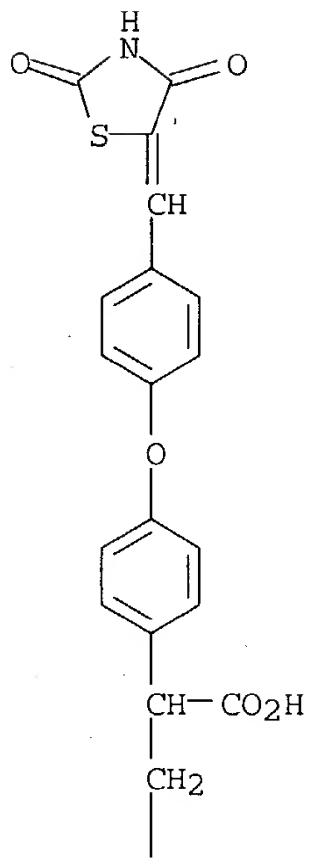


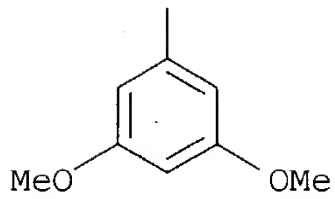
RN 380881-53-8 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A

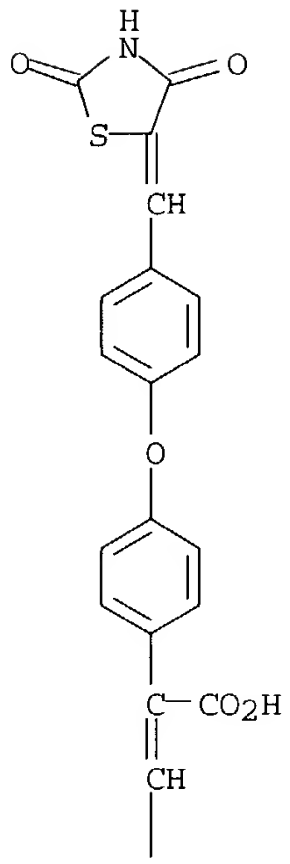


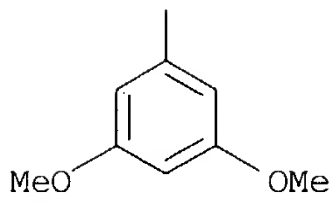
PAGE 2-A



RN 380881-55-0 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]- (9CI) (CA INDEX NAME)

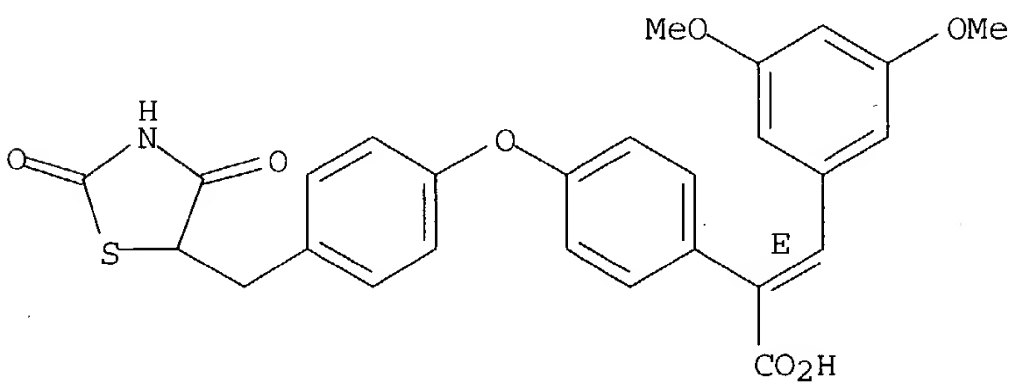
compounds in spec





RN 606932-68-7 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, (αE)- (9CI) (CA INDEX NAME)

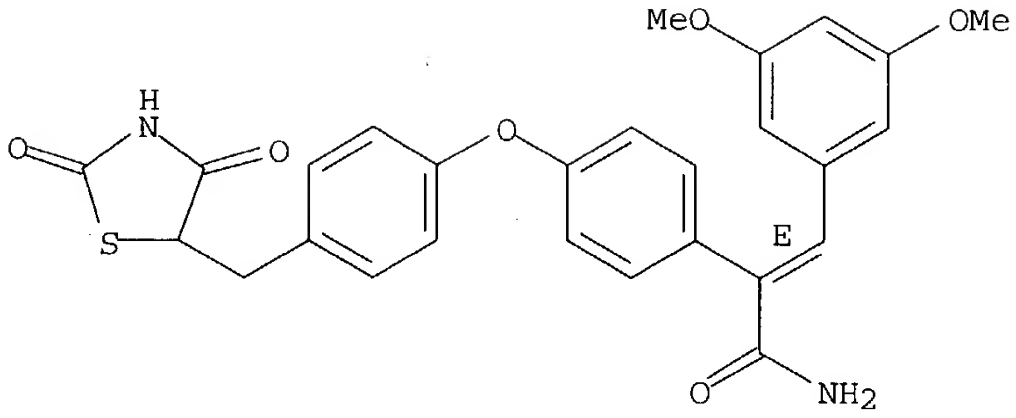
Double bond geometry as shown.



RN 606932-69-8 CAPLUS
CN Benzeneacetamide, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, (αE)- (9CI) (CA INDEX NAME)

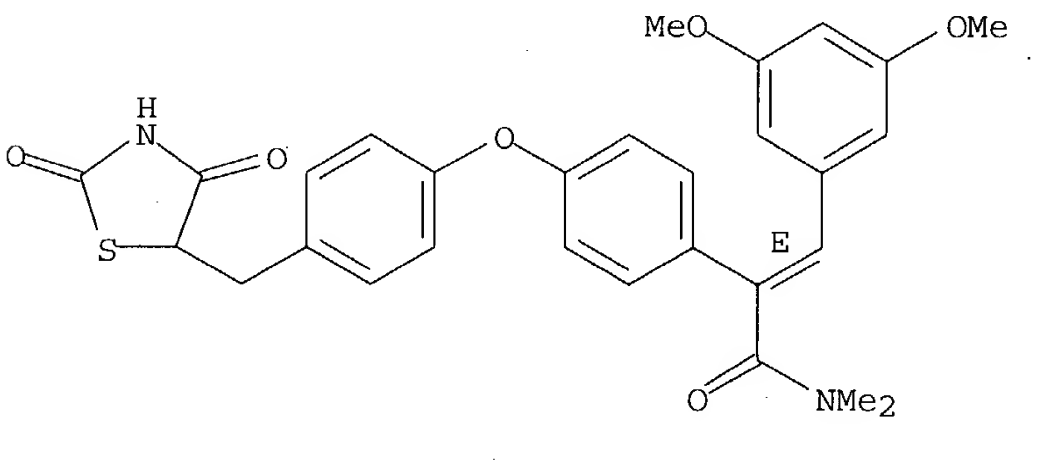
Double bond geometry as shown.

compounds in spec



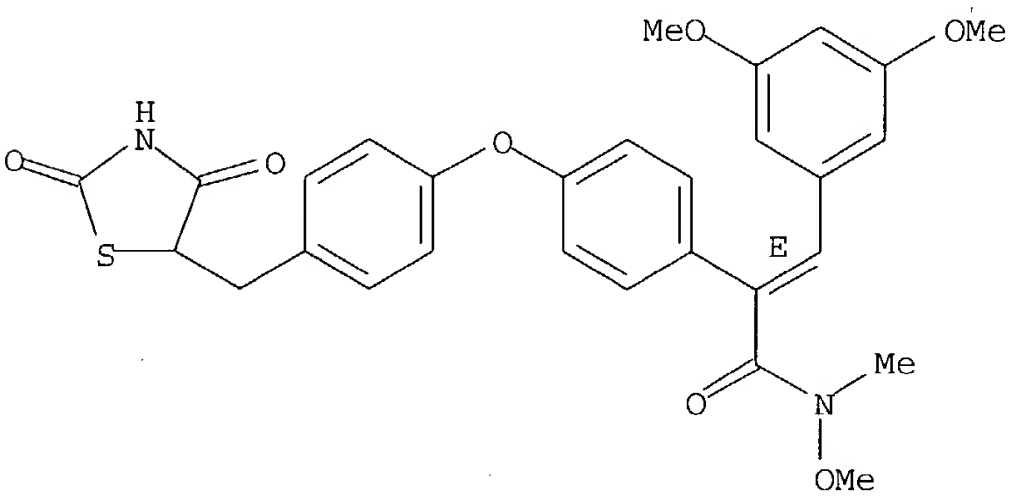
RN 606932-70-1 CAPLUS
CN Benzeneacetamide, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-N,N-dimethyl-, (αE)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 606932-71-2 CAPLUS
CN Benzeneacetamide, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-N-methoxy-N-methyl-, (αE)- (9CI) (CA INDEX NAME)

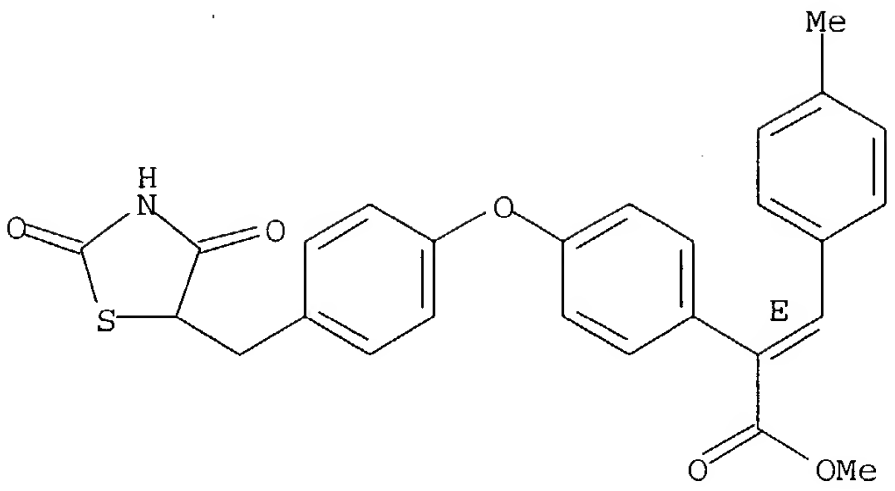
Double bond geometry as shown.



RN 606932-72-3 CAPLUS
CN Benzeneacetic acid, 4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-α-[(4-methylphenyl)methylene]-, methyl ester, (αE)- (9CI) (CA INDEX NAME)

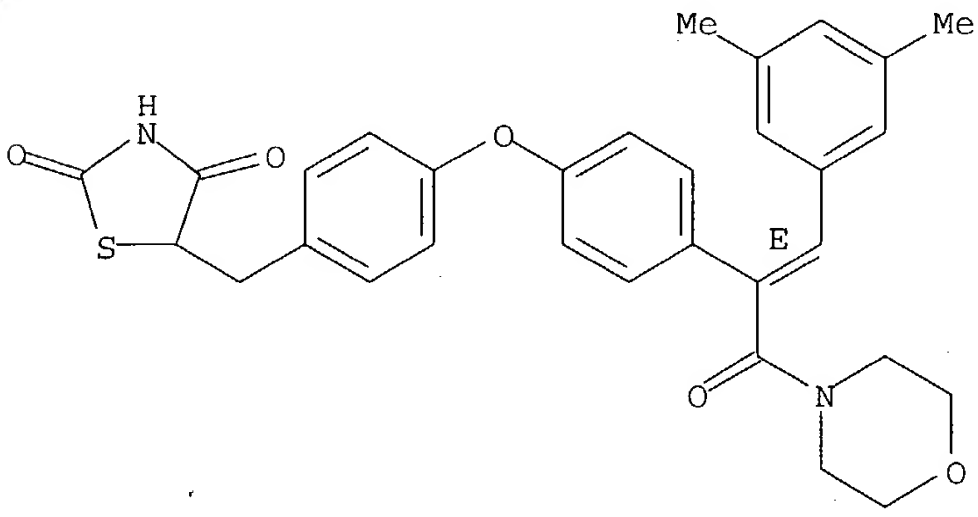
Double bond geometry as shown.

compounds in spec



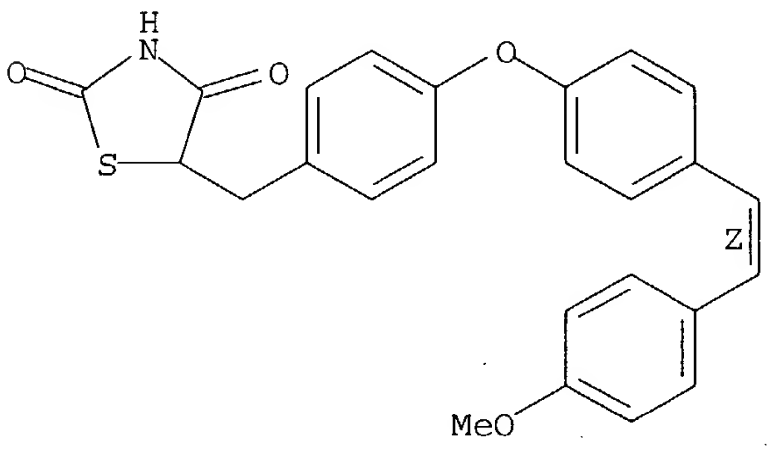
RN 606932-73-4 CAPLUS
CN Morpholine, 4-[(2E)-3-(3,5-dimethylphenyl)-2-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-1-oxo-2-propenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 606932-74-5 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[4-[(1Z)-2-(4-methoxyphenyl)ethenyl]phenoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

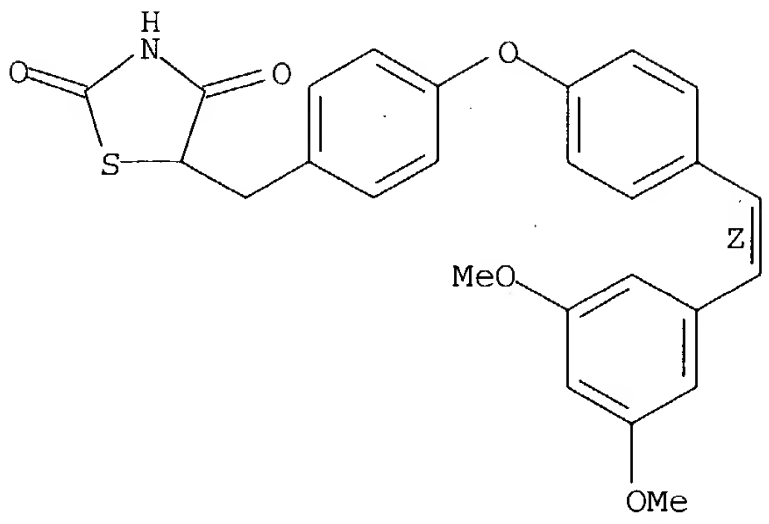
Double bond geometry as shown.



RN 606932-75-6 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[4-[(1Z)-2-(3,5-dimethoxyphenyl)ethenyl]phenoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

compounds in spec

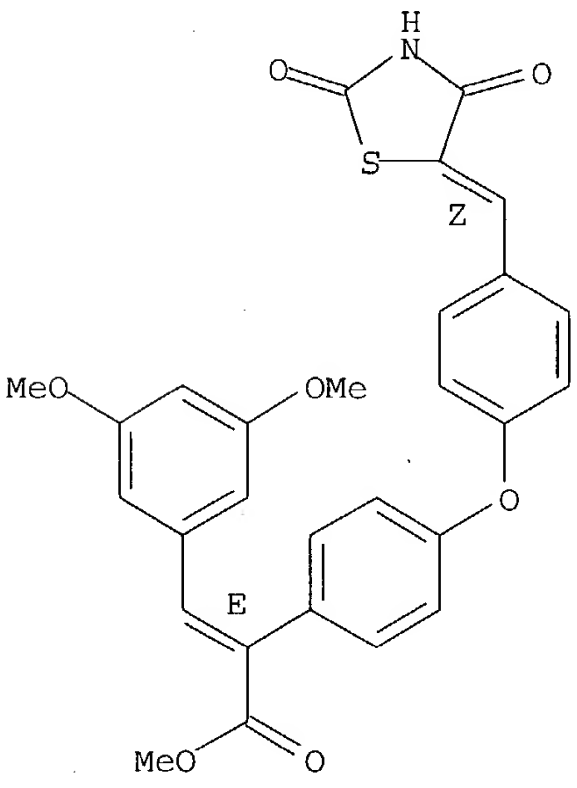
Double bond geometry as shown.



IT **606932-80-3P 606932-81-4P 606932-87-0P**
606932-98-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diphenylethylene compds. containing thiazolidinedione or oxazolidinedione moieties for treating **diabetes**, inflammatory or immunol. disease in combination with other agents)

RN 606932-80-3 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(Z)-(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-, methyl ester, (αE)- (9CI) (CA INDEX NAME)

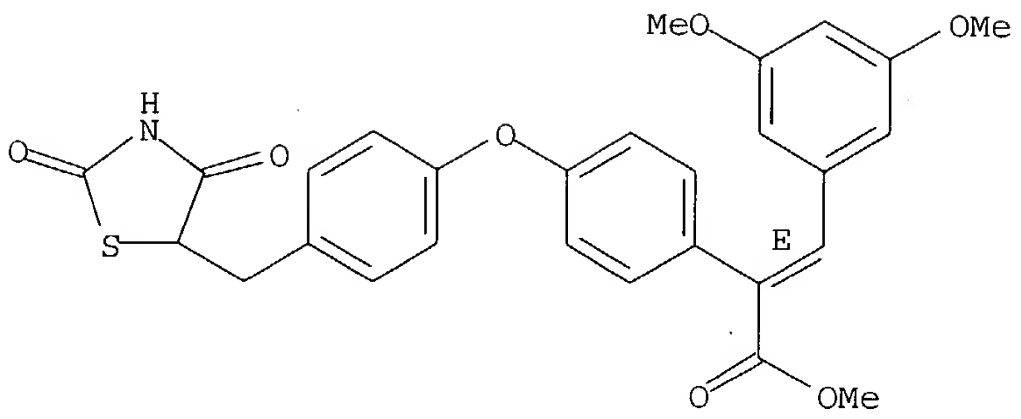
Double bond geometry as shown.



RN 606932-81-4 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester, (αE)- (9CI) (CA INDEX NAME)

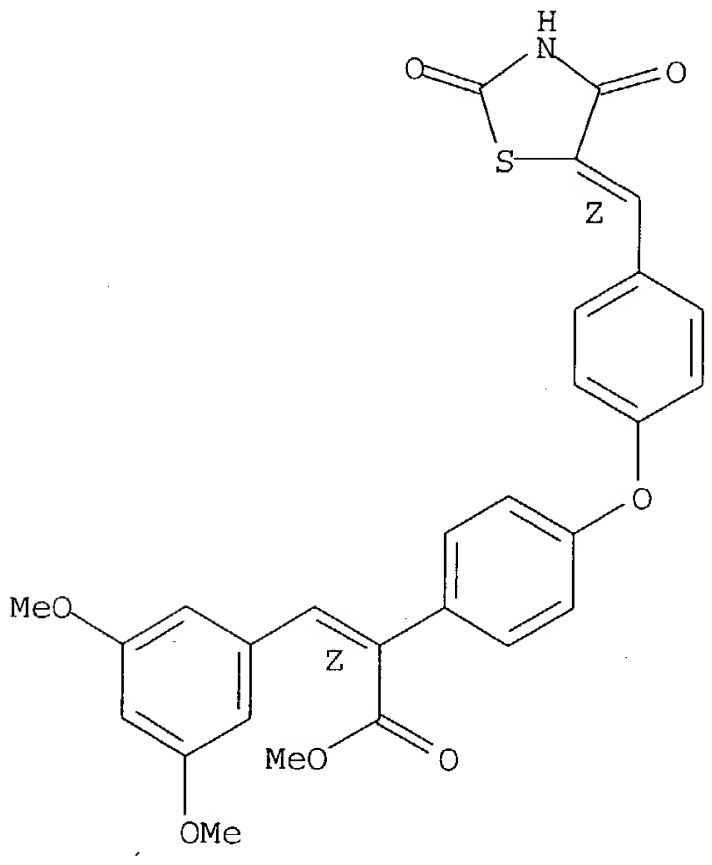
Double bond geometry as shown.

compounds in spec



RN 606932-87-0 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(Z)-(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

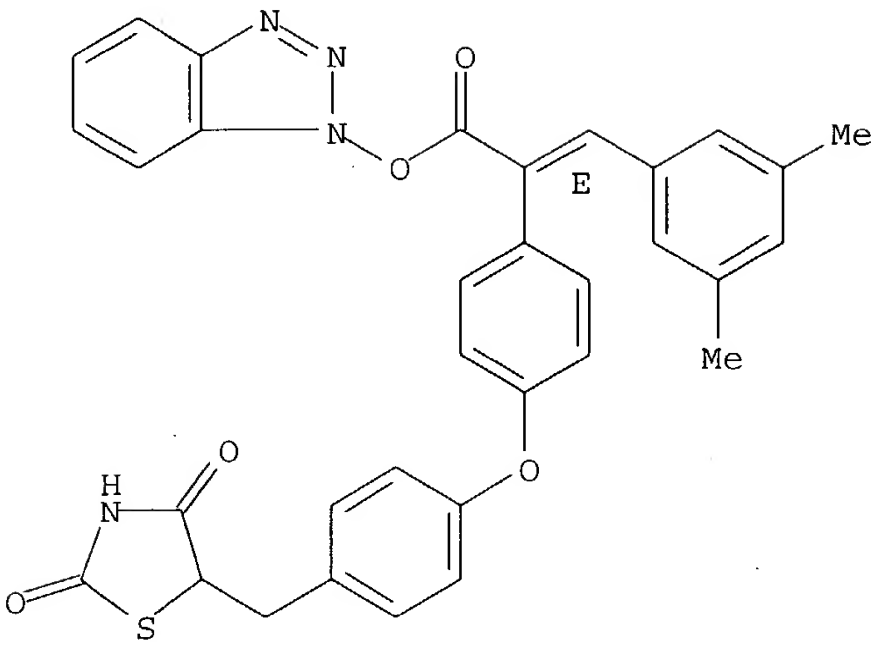
Double bond geometry as shown.



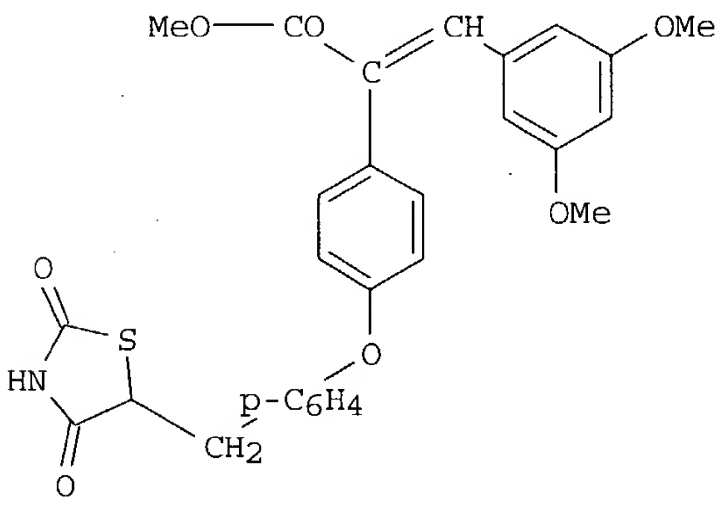
RN 606932-98-3 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[4-[(1E)-1-[(1H-benzotriazol-1-yloxy)carbonyl]-2-(3,5-dimethylphenyl)ethenyl]phenoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

compounds in spec



L6 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:645701 CAPLUS
DN 140:87046
TI Synthesis and structure-Activity relationship studies of cinnamic acid-based novel thiazolidinedione antihyperglycemic agents
AU Neogi, Partha; Lakner, Fredrick J.; Medicherla, Satyanarayana; Cheng, Jin; Dey, Debendranath; Gowri, Maya; Nag, Bishwajit; Sharma, Somesh D.; Pickford, Lesley B.; Gross, Coleman
CS Department of Chemistry, Calyx Therapeutics Inc., Hayward, CA, 94545, USA
SO Bioorganic & Medicinal Chemistry (2003), 11(18), 4059-4067
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 140:87046
GI



I

AB A number of 2,4-thiazolidinedione derivs. of -Ph substituted cinnamic acid were synthesized and studied for their PPAR agonist activity. The E-isomer of cinnamic acid, I, showed moderate PPAR transactivation. The corresponding Z-isomer and double bond reduced derivative were found to be

compounds in spec

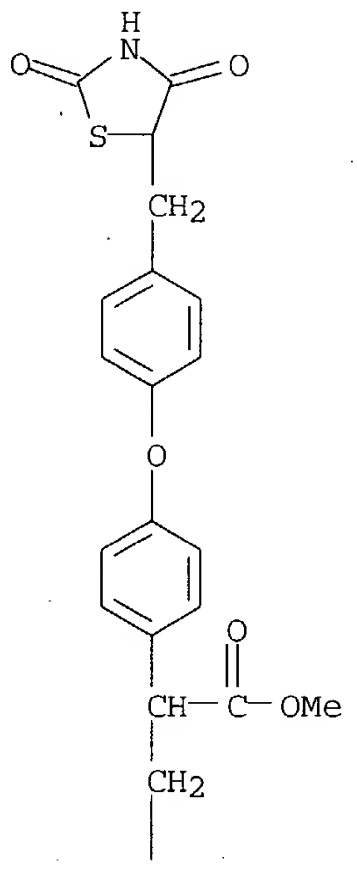
much less potent. Although the E-isomer showed a moderate PPARγ transactivation, it demonstrated a strong glucose-lowering effect in a genetic rodent model of **diabetes**. Results of pharmacokinetic, metabolism and permeability studies are consistent with I being an active prodrug with the hydrolyzed carboxylate as an active metabolite that has similar glucose lowering and PPARγ agonist properties.

IT **380881-51-6P 606932-68-7P 606932-80-3P**
606932-81-4P 606932-84-7P 606932-88-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cinnamic acid-based thiazolidinedione antihyperglycemic agents)

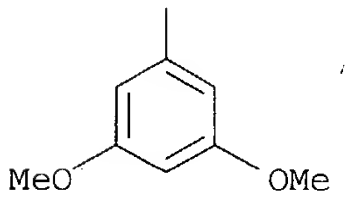
RN 380881-51-6 CAPLUS

CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

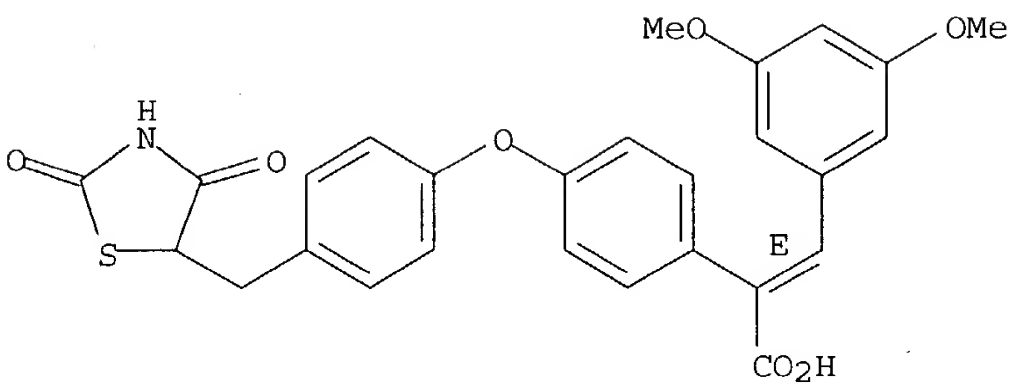


RN 606932-68-7 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, (αE)- (9CI) (CA INDEX NAME)

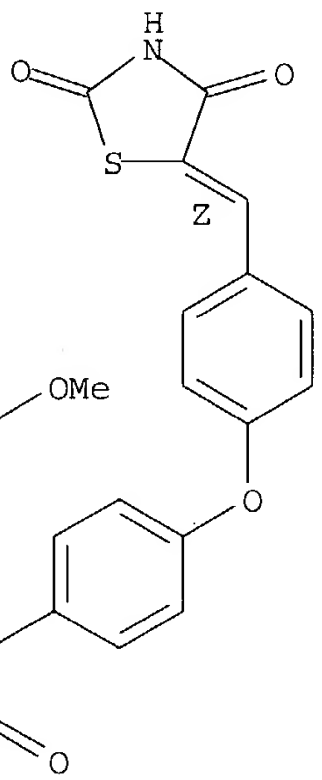
Double bond geometry as shown.

compounds in spec



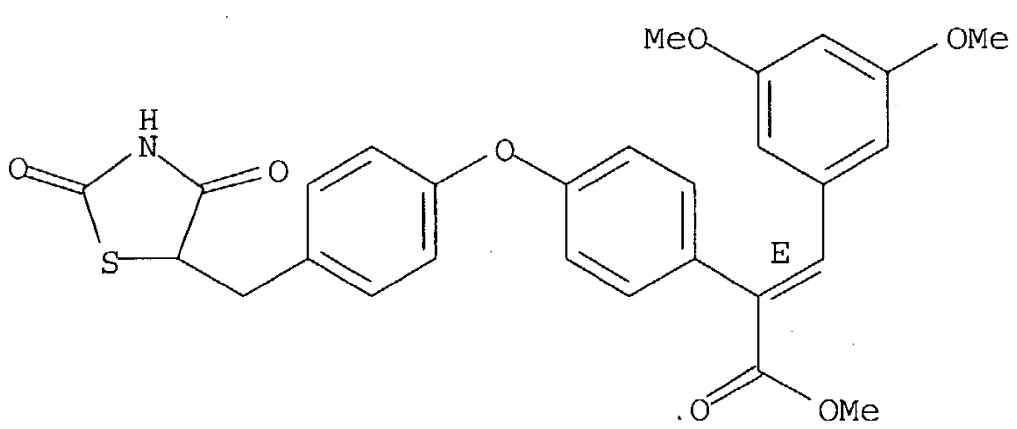
RN 606932-80-3 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(Z)-(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-, methyl ester, (αE)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 606932-81-4 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester, (αE)- (9CI) (CA INDEX NAME)

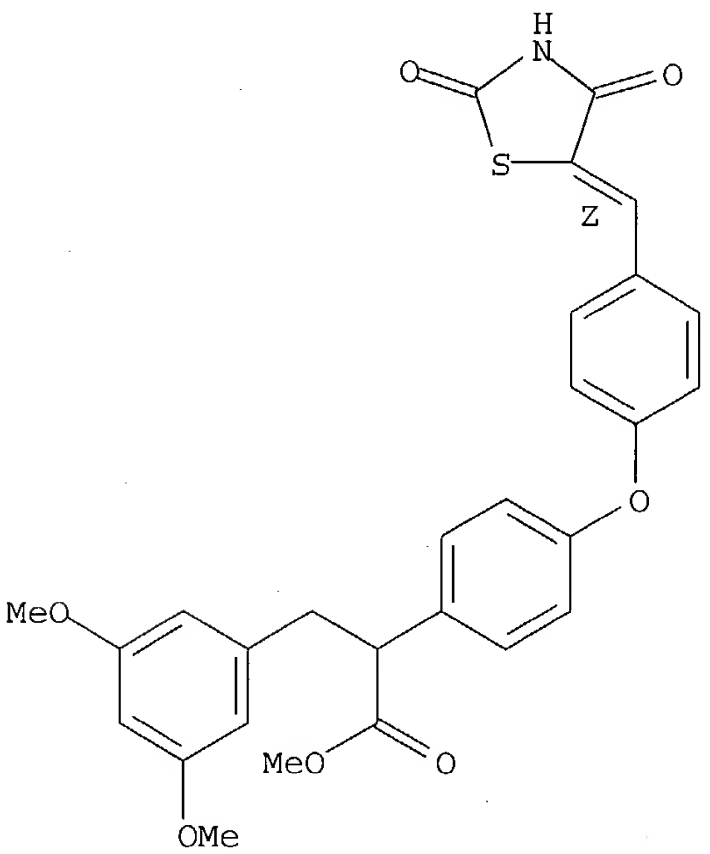
Double bond geometry as shown.



compounds in spec

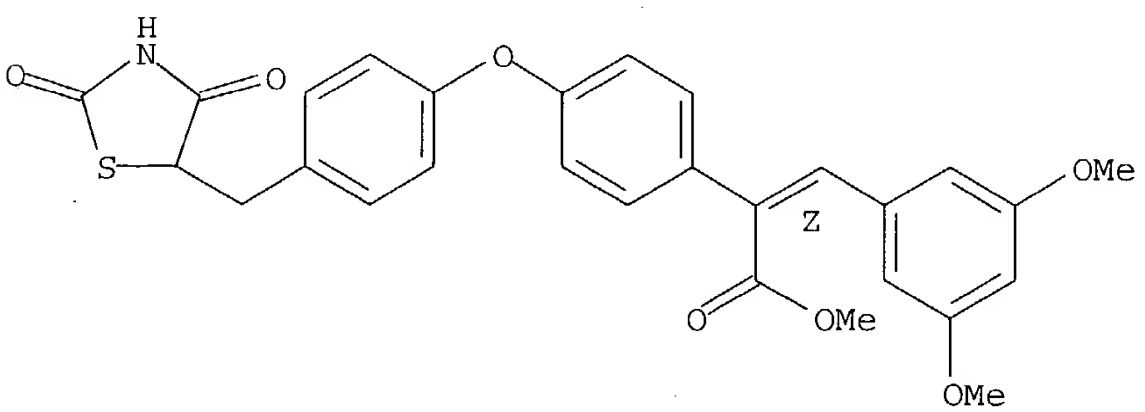
RN 606932-84-7 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(Z)-(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 606932-88-1 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

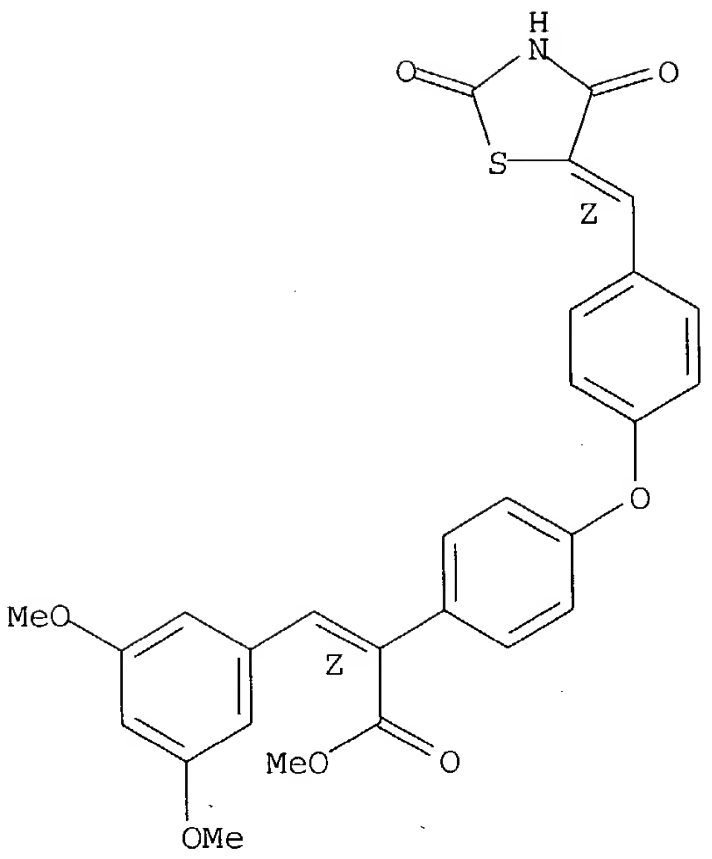
Double bond geometry as shown.



IT **606932-87-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cinnamic acid-based thiazolidinedione antihyperglycemic agents)
RN 606932-87-0 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(Z)-(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

compounds in spec



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:585999 CAPLUS
DN 140:157171
TI A novel peroxisome proliferator-activated gamma (PPARγ) agonist, CLX-0921, has potent antihyperglycemic activity with low adipogenic potential
AU Dey, Debendranath; Medicherla, Satya; Neogi, Partha; Gowri, Maya; Cheng, Jin; Gross, Coleman; Sharma, Somesh D.; Reaven, Gerald M.; Nag, Bishwajit
CS Departments of Biochemistry, Physiology, Chemistry, Clinical Development, and Research Development, Calyx Therapeutics Inc., Hayward, CA, USA
SO Metabolism, Clinical and Experimental (2003), 52(8), 1012-1018
CODEN: METAAJ; ISSN: 0026-0495
PB W. B. Saunders Co.
DT Journal
LA English
AB Agonists of the nuclear receptor peroxisome proliferator-activated receptor gamma (PPARγ) are pharmacol. active antihyperglycemic agents that act by increasing peripheral tissue sensitivity to insulin. Many of these agonists have antihyperglycemic activity that is directly proportional to their ability to bind and activate PPARγ; however, recent data bring this relationship into question. In this report we describe a new PPARγ agonist, CLX-0921, that is derived from a natural product. This thiazolidinedione (TZD) has a spectrum of activity that differs from com. available TZDs. It is a weak activator of PPARγ (EC50 of 0.284 μmol/L) compared to rosiglitazone (EC50 0.009 μmol/L). Despite this difference, the drug maintains potent glucose uptake activity in vitro and glucose-lowering activity in vivo that is equipotent to that of rosiglitazone. Moreover, CLX-0921 showed a 10-fold reduction in in vitro adipogenic potential compared to rosiglitazone. CLX-0921 also increases glycogen synthesis, an activity not typically associated with rosiglitazone or pioglitazone. Thus CLX-0921 appears to have a distinct spectrum of activity relative to other TZDs.
IT **249886-47-3**, CLX 0921

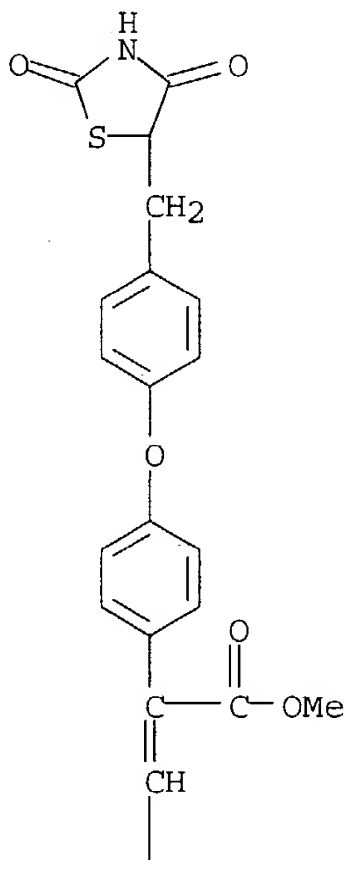
compounds in spec

RL: NPO (Natural product occurrence); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(PPARγ agonist CLX-0921 exhibits antihyperglycemic activity with low adipogenic potential)

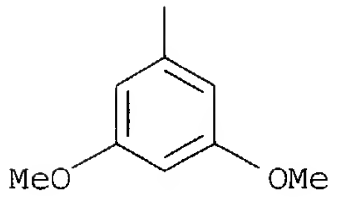
RN 249886-47-3 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:185699 CAPLUS

DN 136:247571

TI Preparation of novel heterocyclic analogs of diphenylethylene compounds as inhibitors of cytokines or cyclooxygenase

IN Nag, Bishwajit; Dey, Debendranath; Medicherla, Satyanarayana; Neogi, Partha

PA USA

SO U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 785,554.
CODEN: USXXCO

DT Patent

compounds in spec

LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002032225	A1	20020314	US 2001-843167	20010427
	US 6245814	B1	20010612	US 1998-74925	19980508
	US 2002025975	A1	20020228	US 2001-785554	20010220
	WO 2001095859	A2	20011220	WO 2001-US17950	20010605
	WO 2001095859	A3	20030828		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001066670	A5	20011224	AU 2001-66670	20010605
	EP 1360178	A2	20031112	EP 2001-944241	20010605
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	JP 2004527455	T2	20040909	JP 2002-510041	20010605
	US 2003181494	A1	20030925	US 2002-265902	20021008
	US 2004186299	A1	20040923	US 2004-808519	20040325
PRAI	US 1998-74925	A2	19980508		
	US 1999-287237	A2	19990406		
	US 2000-591105	A2	20000609		
	US 2001-785554	A2	20010220		
	US 2001-843167	A2	20010427		
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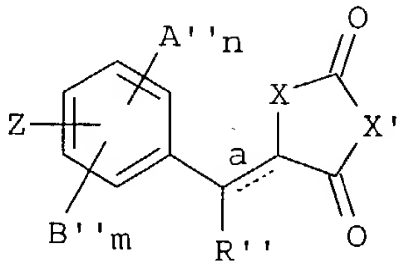
OS MARPAT 136:247571
GI



I

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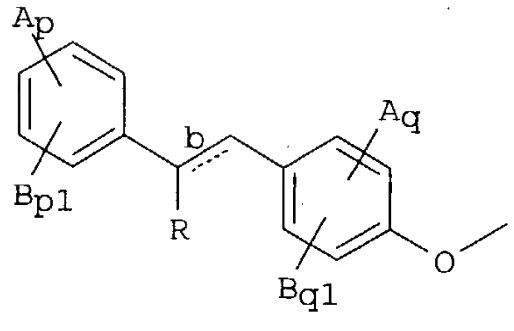

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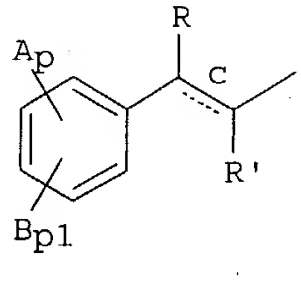


AB Novel diphenylethylene compds. and derivs. thereof containing thiazolidinedione or oxazolidinedione moieties are provided which are effective in lowering blood glucose level, serum insulin, triglyceride and

compounds in spec

free fatty acid levels in animal models of Type II **diabetes**. The above compds. and their derivs. are resented by formula [I; Z = Q, Q1, H, A", B"; wherein n, m, q, q1 = integers from zero to 4 provided that n+m≤4 and q+q1≤4; p, p1 = integers from zero to 5 provided that p+p1≤5; a, b and c are double bonds which may be present or absent; when present; the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S-configuration; R, R', R" = H, C1-20 linear or branched alkyl, C2-20 linear or branched alkenyl, CO2Z' (wherein Z' = H, Na, K, or other pharmaceutically acceptable counterion such as Ca, Mg, ammonium, tromethamine, and the like), CO2R''', NH2, NHR''', N(R''')2, OH, OR''', halo, substituted C1-20 linear or branched alkyl or substituted C2-20 linear or branched alkenyl (wherein R''' is C1-20 linear or branched alkyl or linear or branched alkenyl); A, A', A'' = H, C1-20 acylamino, C1-20 acyloxy, C1-20 alkanoyl, C1-20 alkoxycarbonyl, C1-20 alkoxy, C1-20 alkylamino, C1-20 alkylcarboxylamino, CO2H, cyano, halo, HO; B, B', B'' = H, C1-20 acylamino, C1-20 acyloxy, C1-20 alkanoyl, C1-20 alkenoyl, C1-20 alkoxycarbonyl, C1-20 alkoxy, C1-20 alkylamino, C1-20 alkylcarboxylamino, aroyl, aralkanoyl, CO2H, cyano, halo, HO; or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR''', O or S]. In contrast to previously reported thiazolidinedione compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity. They inhibit the activity of TNF-alpha, interleukin IL-1 or IL-6 or cyclooxygenase-2 (COX-2). The compds. are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis. Thus, To a mixture of 3,5-dimethoxybenzaldehyde (500 g) and p-hydroxyphenylacetic acid (457 g) was added acetic anhydride (1 L) and triethylamine (420 mL) and the nonhomogeneous mixture on heating became homogeneous at 70° and stirred at 130-140° for 6 h to give 47% 3-(3,5-dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid (II) (428 g). II (427.5 g) was suspended in 3 L methanol, treated with 100 mL concentrated H2SO4, and heated at reflux for 20 h under Ar to give 97% 3-(3,5-dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid Me ester (III). III (433 g) was dissolved in 1.6 L DMF, treated with 60.4 g NaH (50% in oil) and the with 185 mL p-fluorobenzaldehyde, and heated at 180° for 18 h to give 77% 3-(3,5-dimethoxyphenyl)-2-[4-(4-formylphenoxy)phenyl]acrylic acid Me ester which (352 g), 2,4-thiazolidinedione 98.6, benzoic acid 134, and piperidine 107.4 g were heated in 2.5 L toluene at reflux with continuous removal of H2O through Dean-Stark apparatus to give 86% 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]acrylic acid Me ester (IV). IV (30 g) was hydrogenated over 15 g 10% Pd-C in 900 mL dioxane in a Parr apparatus at 60 Psi for 24 h, followed by adding 15 g 10% Pd-C and continuing the hydrogenation for another 24 h to give 86% 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]acrylic acid Me ester (V). When V was orally administered to ob/ob mice with a single oral dose (50 mg/kg body weight), there was a 62 % drop in blood glucose level and, similar to db/db mice, there was no significant increase in body weight between the control and the treatment groups. This was in contrast to treatment of diabetic animals by thiazolidinedione type compds. which are known to be associated with increase in body weight

IT **249886-47-3P**, 5-[4-[4-[1-Carbomethoxy-2-(3,5-dimethoxyphenyl)ethenyl]phenoxy]benzyl]-2,4-thiazolidinedione
380881-31-2P, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]acrylic acid methyl ester
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL

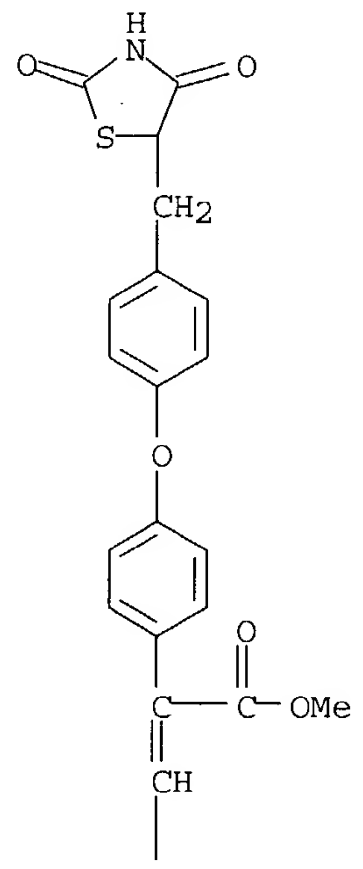
compounds in spec

(Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of novel heterocyclic analogs of phenylethylene compds. as inhibitors of cytokines or cyclooxygenase for therapeutic agents)

RN 249886-47-3 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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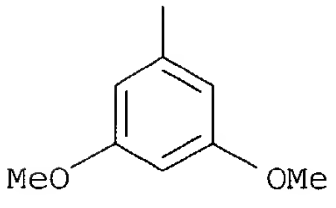
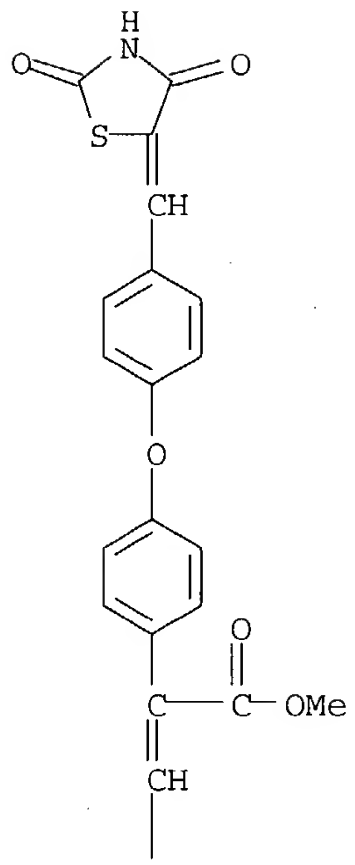


RN 380881-31-2 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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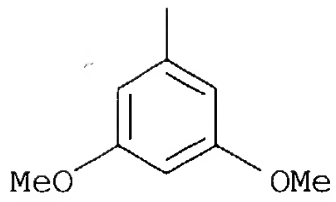
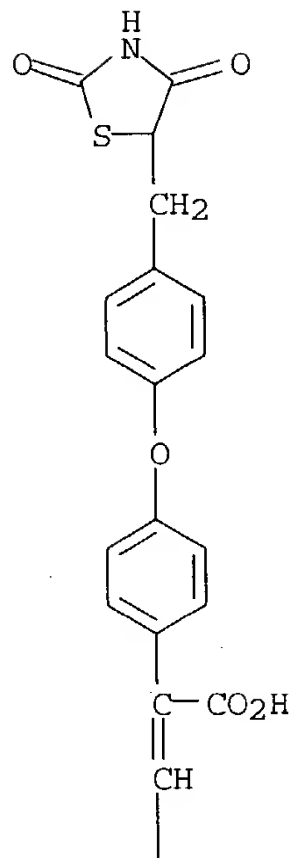


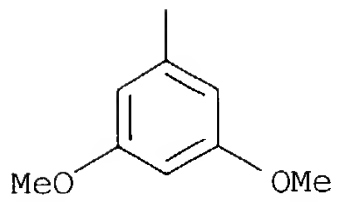
IT **380881-35-6P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]acrylic acid
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of novel heterocyclic analogs of phenylethylene compds. as inhibitors of cytokines or cyclooxygenase for therapeutic agents)

RN 380881-35-6 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]- (9CI) (CA INDEX NAME)

compounds in spec





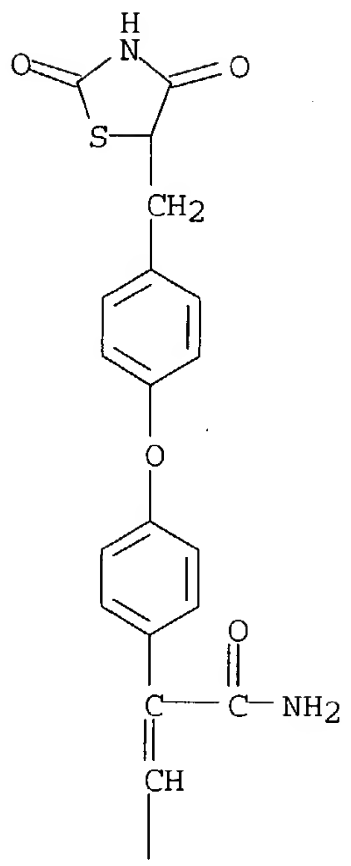
IT **380881-37-8P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]acrylamide **380881-39-0P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]-N,N-dimethylacrylamide **380881-41-4P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]-N-methoxy-N-methylacrylamide **380881-47-0P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]propionic acid methyl ester **380881-49-2P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]propionic acid **380881-51-6P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]propionic acid methyl ester **380881-53-8P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]propionic acid **380881-55-0P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]acrylic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel heterocyclic analogs of phenylethylene compds. as inhibitors of cytokines or cyclooxygenase for therapeutic agents)

RN 380881-37-8 CAPLUS

CN Benzeneacetamide, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]- (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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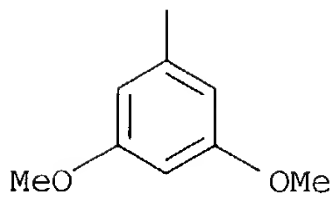
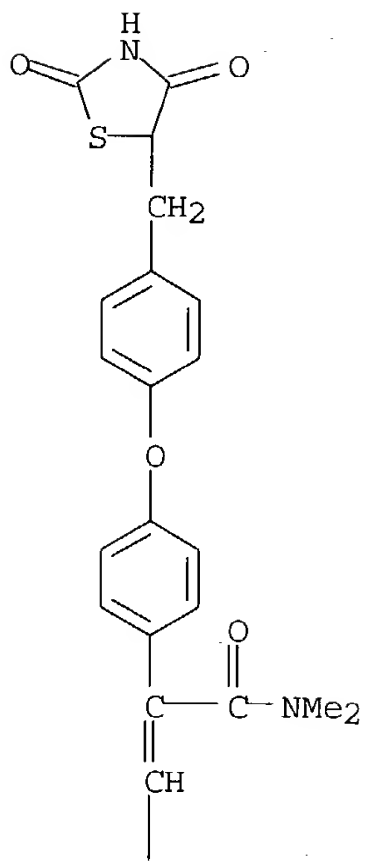


RN 380881-39-0 CAPLUS
CN Benzeneacetamide, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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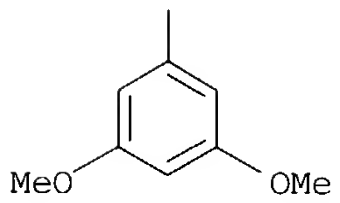
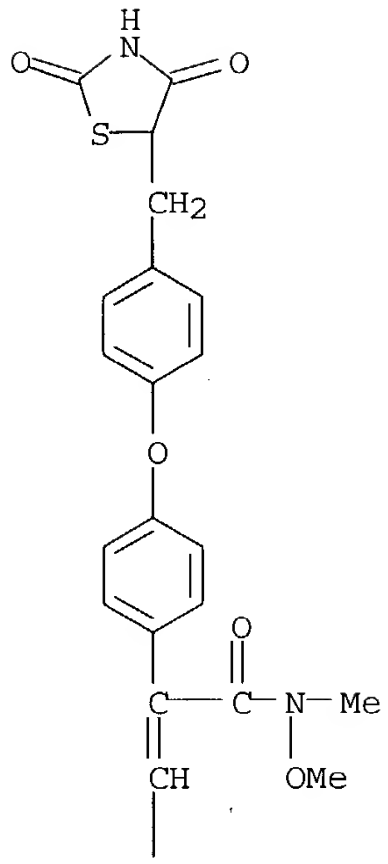
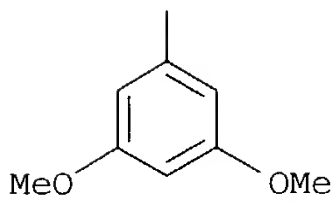


RN 380881-41-4 CAPLUS
CN Benzeneacetamide, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-N-methoxy-N-methyl- (9CI) (CA INDEX NAME)

compounds in spec

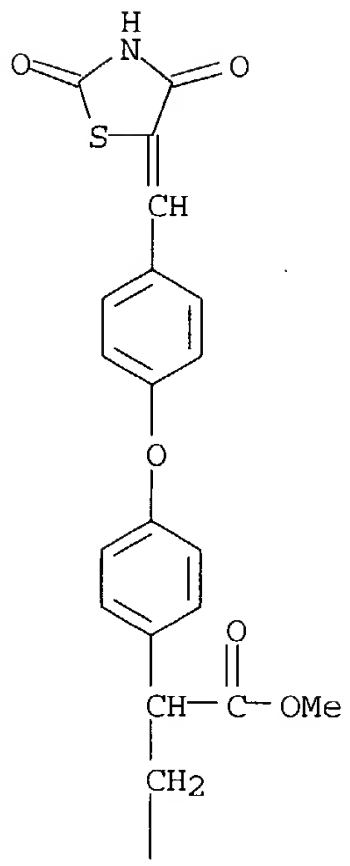




RN 380881-47-0 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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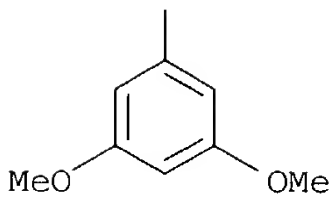
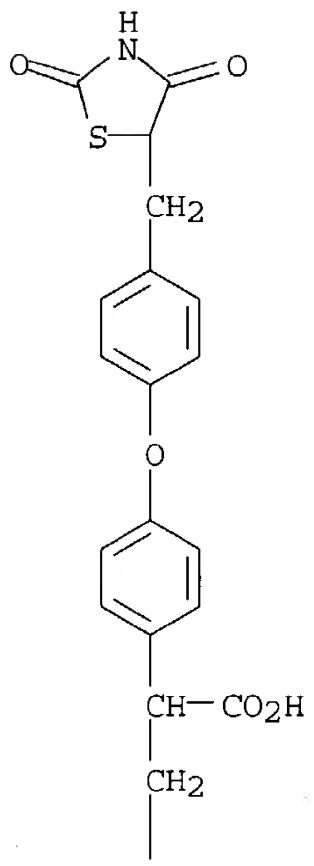


RN 380881-49-2 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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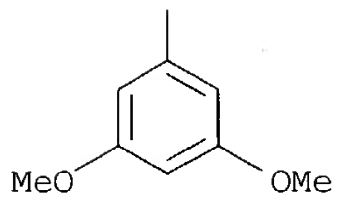
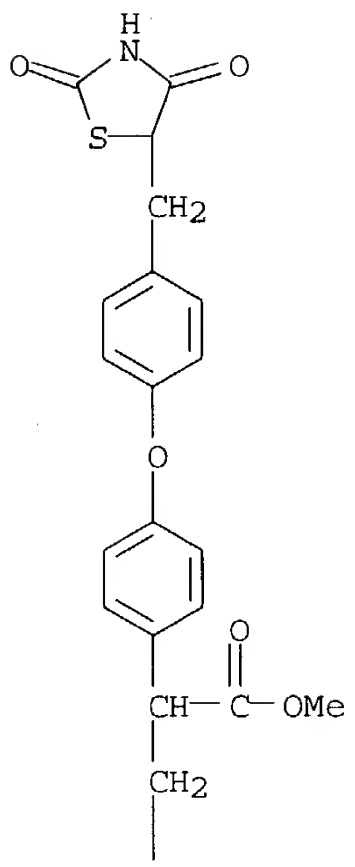
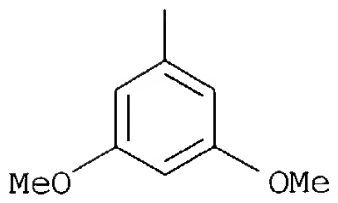


RN 380881-51-6 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

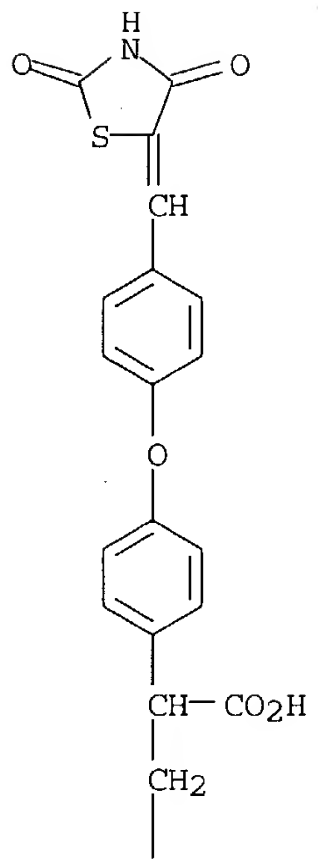
compounds in spec

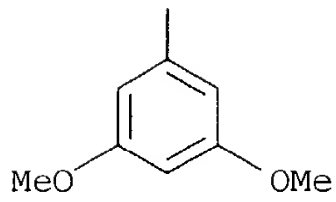




RN 380881-53-8 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)

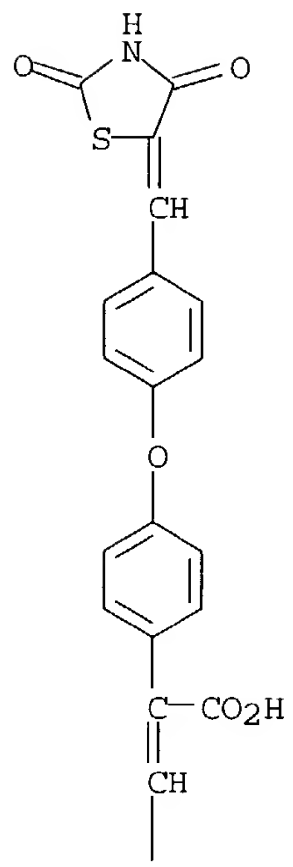
compounds in spec

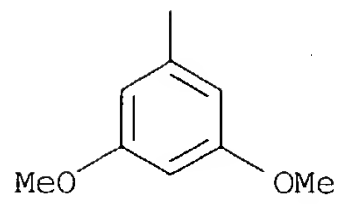




RN 380881-55-0 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]- (9CI) (CA INDEX NAME)

compounds in spec





L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:158391 CAPLUS
DN 136:216745
TI Preparation and activity of diphenylethylene thiazolidinediones and analogs as antidiabetics, antiinflammatories, or immunomodulators
IN Nag, Bishwajit; Dey, Debendranath; Medicherla, Satyanarayana; Neogi, Partha
PA USA
SO U.S. Pat. Appl. Publ., 30 pp., Cont.-in-part of U.S. Ser. No. 591,105.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 9

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PI	US 2002025975	A1	20020228	US 2001-785554	20010220
	US 6245814	B1	20010612	US 1998-74925	19980508
	US 2002032225	A1	20020314	US 2001-843167	20010427
	WO 2001095859	A2	20011220	WO 2001-US17950	20010605
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compounds in spec

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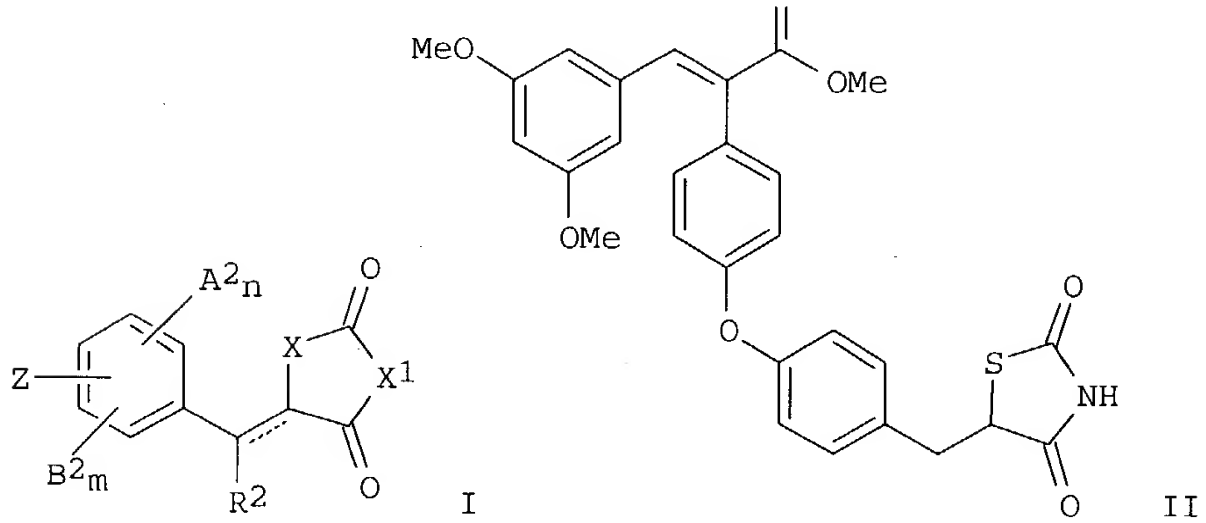
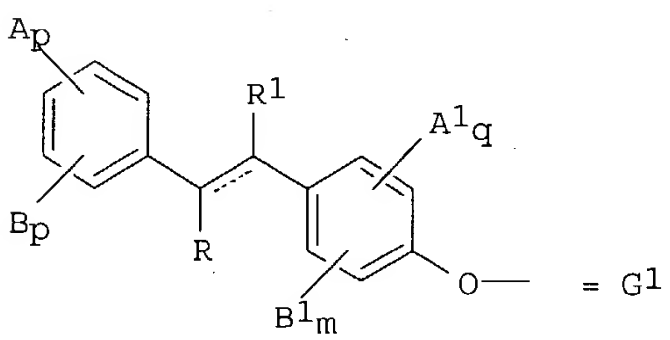


I II



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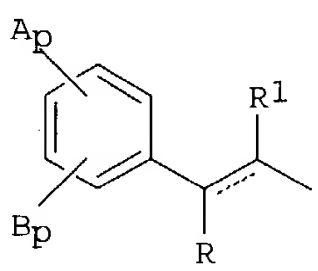


= G2

AB Title compds. I [wherein Z = G1, H, A2, B2, or G2; n, m, and q = independently 0-4; p = independently 0-5; R, R1, and R2 = independently H, (un)substituted alkyl or alkenyl, CO2Z1, CO2R3, NH2, NHR3, NR32, OH, OR3, or halo; Z1 = H, Na, K, or other pharmaceutically acceptable counterion; R3 = alkyl or alkenyl; A, A1, and A2 = independently H, acylamino, acyloxy, alkanoyl, alkoxycarbonyl, alkoxy, alkylamino, alkylcarboxylamino, carboxyl, CN, H, or OH; B, B1, and B2 = independently H, acylamino,

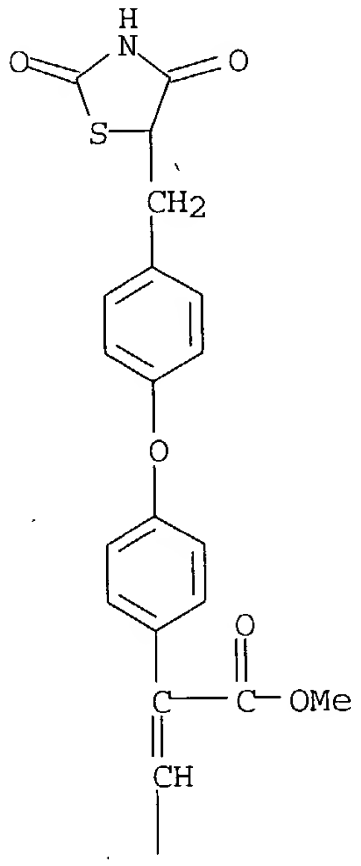
compounds in spec

acyloxy, alkanoyl, alkenoyl, alkoxycarbonyl, alkoxy, alkylamino, alkylcarboxylamino, aroyl, aralkanoyl, carboxyl, CN, halo, or OH; or A and B or A1 and B1 or A2 and B2 together form a methylenedioxy or ethylenedioxy group; X and X1 = independently NH, NR3, O, or S] are provided which are effective in lowering blood glucose level, serum insulin, triglyceride, and free fatty acid levels in animal models of Type II **diabetes**. In contrast to previously reported thiazolidinedione compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity. Thus, II was prepared in five steps by condensation of 3,5-dimethoxybenzaldehyde with 4-hydroxyphenylacetic acid (47%), followed by esterification (97%), etherification with 4-fluorobenzaldehyde (77%), condensation with 2,4-thiazolidinedione (86%), and hydrogenation of the ylidene double bond (40%). Oral administration of II to obese mice caused a 62% drop in blood glucose level. I are useful for the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer, and multiple sclerosis.

IT **249886-47-3P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and activity of diphenylethylene thiazolidinediones and analogs as antidiabetics, antiinflammatories, or immunomodulators)

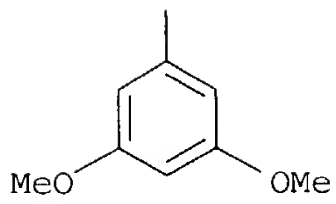
RN 249886-47-3 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



compounds in spec

PAGE 2-A

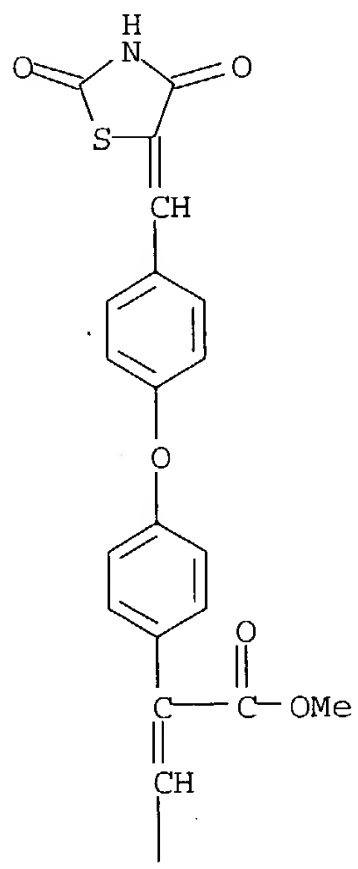


IT **380881-31-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and activity of diphenylethylene thiazolidinediones and analogs as antidiabetics, antiinflammatories, or immunomodulators)

RN 380881-31-2 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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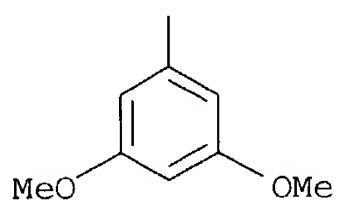

L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:923567 CAPLUS

DN 136:37596

TI Preparation and activity of diphenylethylene thiazolidinedione or

compounds in spec

oxazolidinedione compounds as antidiabetics or antiinflammatories

IN Neogi, Partha; Nag, Bishwajit; Medicherla, Satyanarayana; Dey, Debendranath

PA Calyx Therapeutics, Inc., USA

SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001095859	A2	20011220	WO 2001-US17950	20010605
	WO 2001095859	A3	20030828		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	AU 2001066670	A5	20011224	AU 2001-66670	20010605
	EP 1360178	A2	20031112	EP 2001-944241	20010605
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OS MARPAT 136:37596

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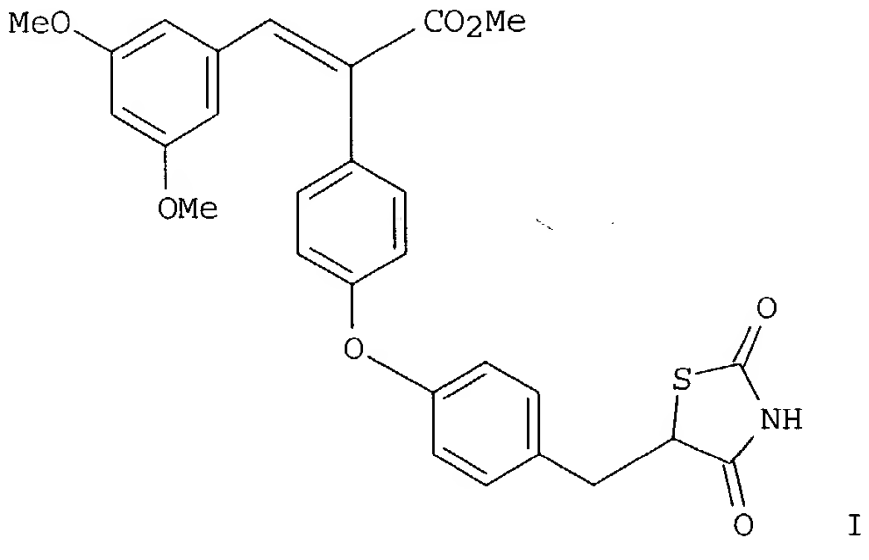

I

AB Novel diphenylethylene compds. and derivs. thereof containing thiazolidinedione or oxazolidinedione moieties are provided which are

compounds in spec

effective in lowering blood glucose level, serum insulin, triglyceride and free fatty acid levels in animal models of Type II **diabetes**. In contrast to previously reported thiazolidinedione compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity. Thus, (I) was prepared in five steps by condensation of 3,5-dimethoxybenzaldehyde with 4-hydroxyphenylacetic acid followed by esterification and etherification with 4-fluorobenzaldehyde and condensation with 2,4-thiazolidinedione and hydrogenation of the ylidene double bond. Oral administration of I to obese mice caused a 62% drop in blood glucose level. The compds. are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis.

IT **249886-47-3P 380881-31-2P 380881-35-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and activity of diphenylethylene thiazolidinedione or oxazolidinedione compds. as antidiabetics or antiinflammatories)

RN 249886-47-3 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

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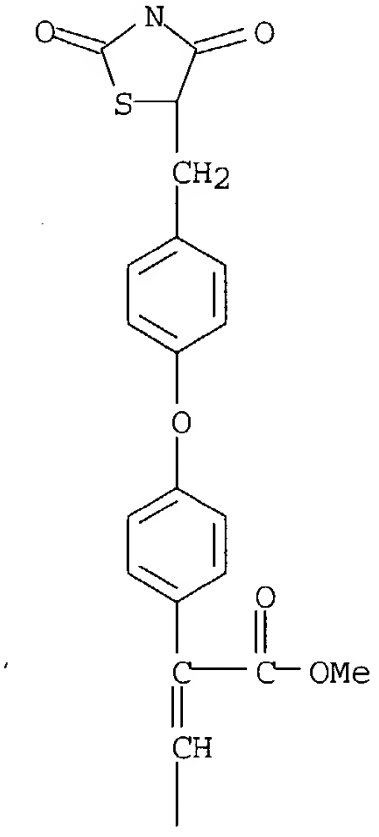

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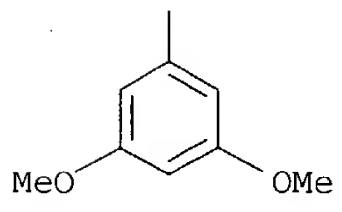
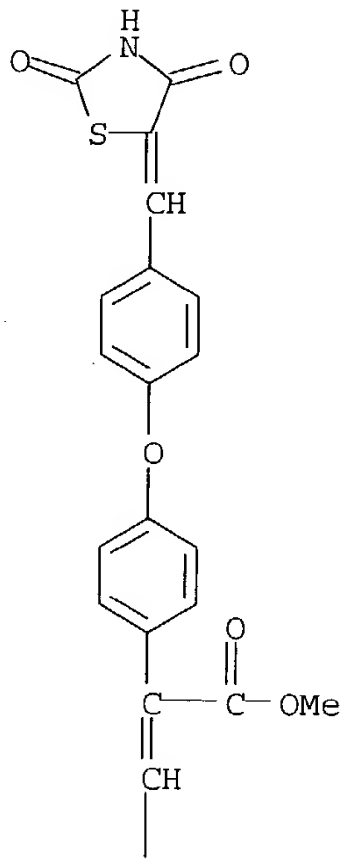


compounds in spec

RN 380881-31-2 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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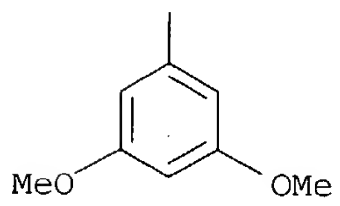
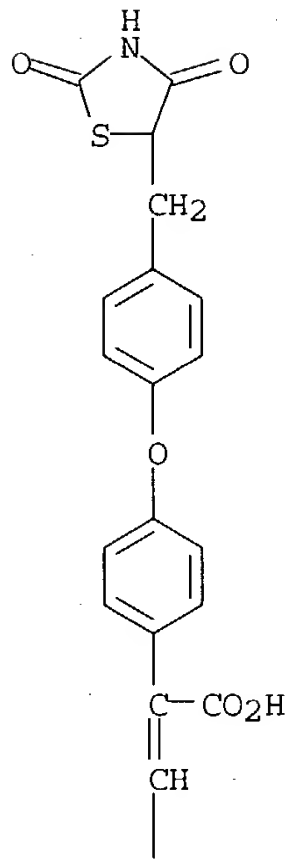
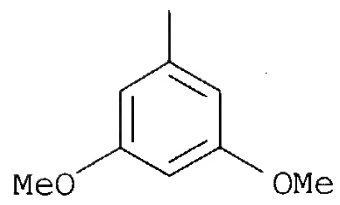


RN 380881-35-6 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]- (9CI) (CA INDEX NAME)

compounds in spec



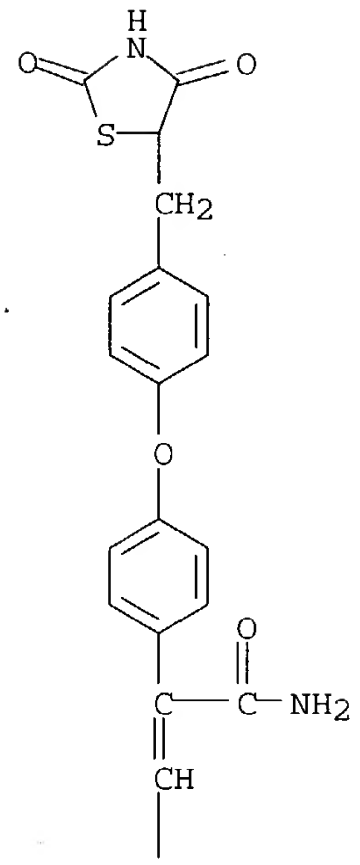


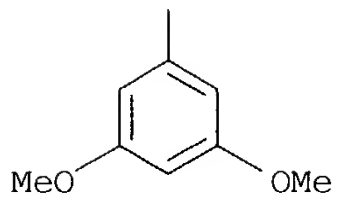
IT **380881-37-8P 380881-39-0P 380881-41-4P**
380881-47-0P 380881-49-2P 380881-51-6P
380881-53-8P 380881-55-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and activity of diphenylethylene thiazolidinedione or oxazolidinedione compds. as antidiabetics or antiinflammatories)

RN 380881-37-8 CAPLUS

CN Benzeneacetamide, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]- (9CI) (CA INDEX NAME)

compounds in spec

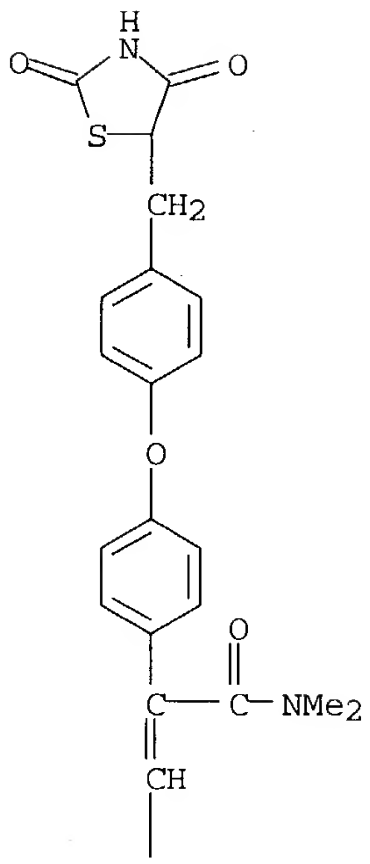




RN 380881-39-0 CAPLUS
CN Benzeneacetamide, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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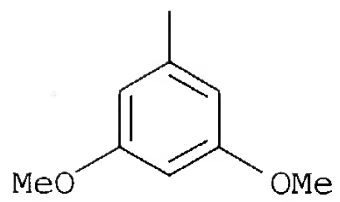
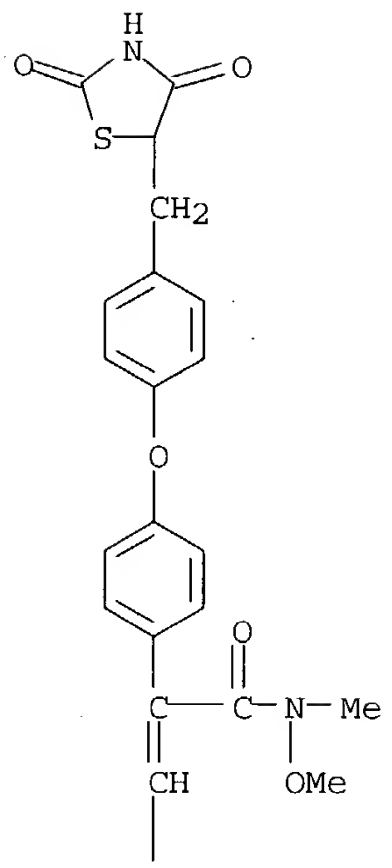


RN 380881-41-4 CAPLUS
CN Benzeneacetamide, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-N-methoxy-N-methyl- (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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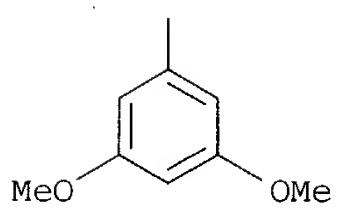
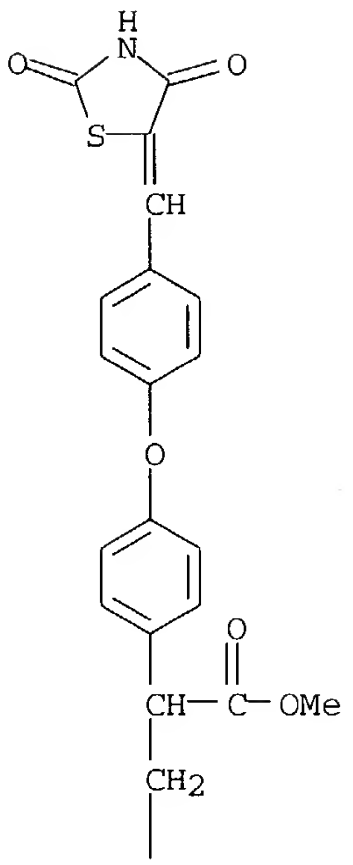


RN 380881-47-0 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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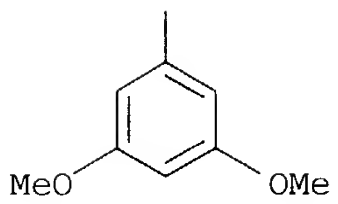
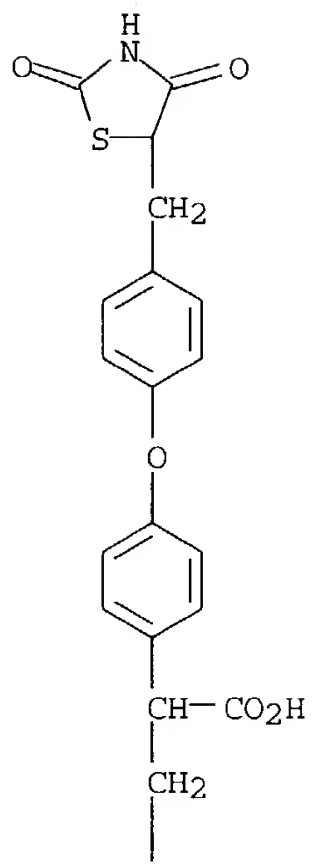


RN 380881-49-2 CAPLUS

CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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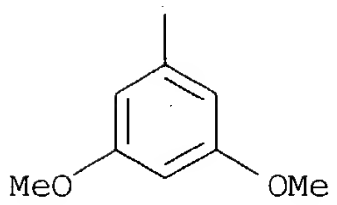
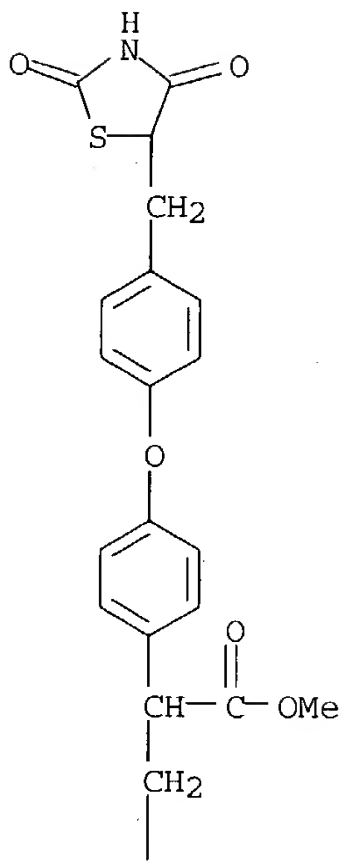


RN 380881-51-6 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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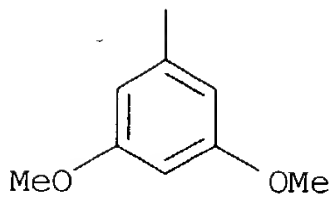
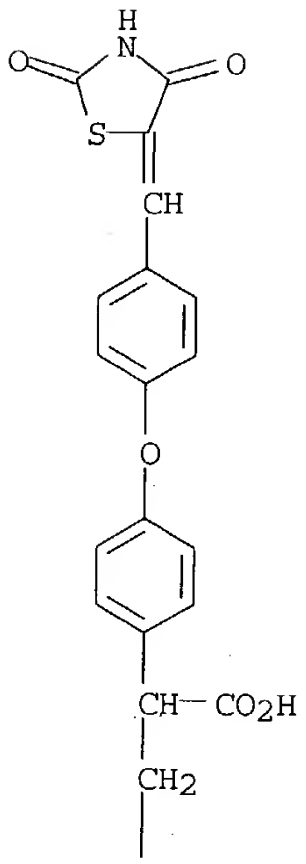


RN 380881-53-8 CAPLUS

CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)

compounds in spec

PAGE 1-A



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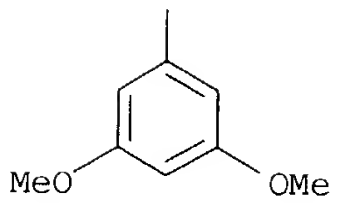
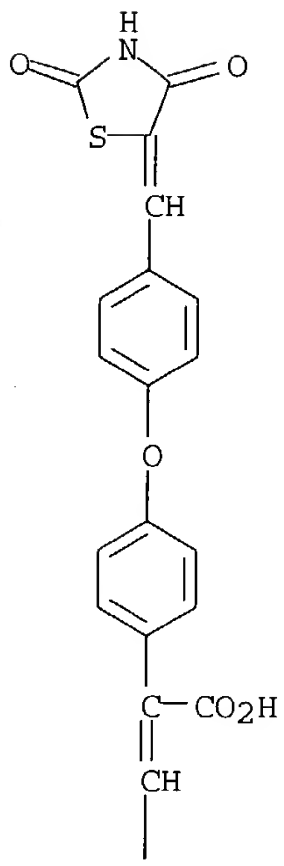
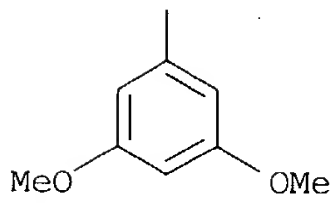


RN 380881-55-0 CAPLUS
CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]- (9CI) (CA INDEX NAME)

compounds in spec





L6 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:736478 CAPLUS
DN 131:332116
TI Heterocyclic analogs of diphenylethylene compounds for the treatment of **diabetes**
IN Neogi, Partha; Nag, Bishwajit; Medicherla, Satyanarayana; Dey, Debendranath
PA Calyx Therapeutics, Inc., USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 9

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9958127	A1	19991118	WO 1999-US9982	19990507

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,

compounds in spec

	CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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AU 9939741	A1	19991129	AU 1999-39741	19990507
AU 751235	B2	20020808		
EP 1007039	A1	20000614	EP 1999-922836	19990507
EP 1007039	B1	20040303		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
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AT 260906	E	20040315	AT 1999-922836	19990507
PRAI US 1998-74925	A	19980508		
US 1999-287237	A	19990406		
WO 1999-US9982	W	19990507		

OS MARPAT 131:332116

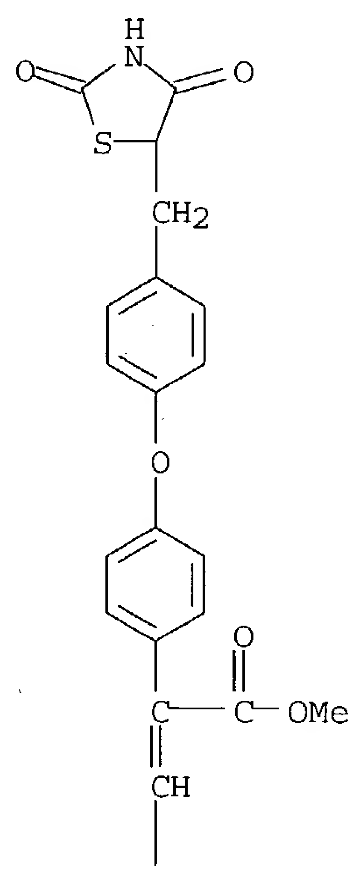
AB Diphenylethylene compds. containing thiazolidinedione or oxazolidinedione moieties are provided which are effective in lowering blood glucose level, serum insulin, triglyceride and free fatty acid levels in animal models of Type II **diabetes**. In contrast to previously reported thiazolidine compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity.

IT **249886-47-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic analogs of diphenylethylene compds. for treatment of **diabetes**)

RN 249886-47-3 CAPLUS

CN Benzeneacetic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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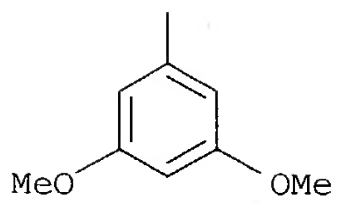

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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compounds in spec

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L3 14 S L1 FUL

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L6 3 S L5 AND L4

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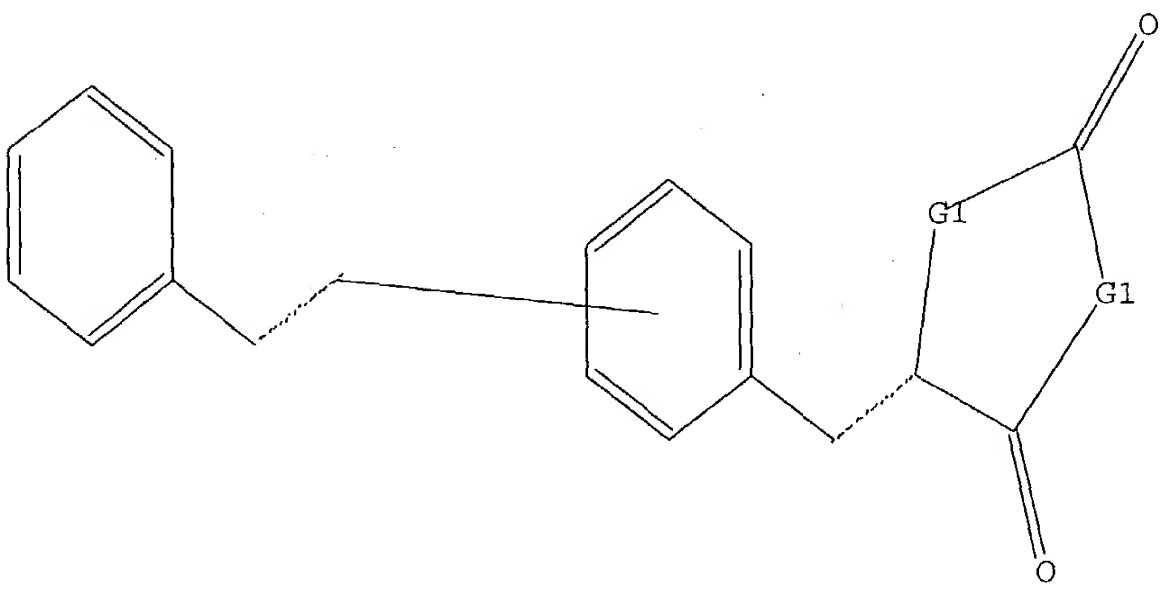

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Structure attributes must be viewed using STN Express query preparation.

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L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:566933 CAPLUS
DN 141:270985
TI Three-Dimensional Quantitative Structure-Activity Relationship Analysis of a Set of Plasmodium falciparum Dihydrofolate Reductase Inhibitors Using a Pharmacophore Generation Approach
AU Parenti, Marco Daniele; Pacchioni, Sara; Ferrari, Anna Maria; Rastelli, Giulio
CS Dipartimento di Scienze Farmaceutiche, Universita di Modena e Reggio Emilia, Modena, 41100, Italy
SO Journal of Medicinal Chemistry (2004), 47(17), 4258-4267
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A 3D pharmacophore model able to quant. predict inhibition consts. was derived for a series of inhibitors of Plasmodium falciparum dihydrofolate

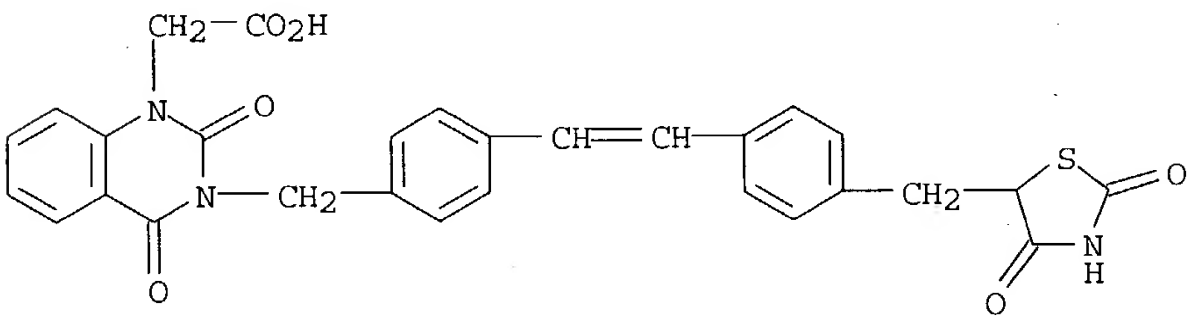
compounds in spec

reductase (PfDHFR), a validated target for antimalarial therapy. The data set included 52 inhibitors, with 23 of these comprising the training set and 29 an external test set. The activity range, expressed as Ki, of the training set mols. was from 0.3 to 11 300 nM. The 3D pharmacophore, generated with the HypoGen module of Catalyst 4.7, consisted of two hydrogen bond donors, one pos. ionizable feature, one hydrophobic aliphatic feature, and one hydrophobic aromatic feature and provided a 3D-QSAR model with a correlation coefficient of 0.954. Importantly, the type and spatial location of the chemical features encoded in the pharmacophore were in full agreement with the key binding interactions of PfDHFR inhibitors as previously established by mol. modeling and crystallog. of enzyme-inhibitor complexes. The model was validated using several techniques, namely, Fisher's randomization test using CatScramble, leave-one-out test to ensure that the QSAR model is not strictly dependent on one particular compound of the training set, and activity prediction in an external test set of compds. In addition, the pharmacophore was able to correctly classify as active and inactive the dihydrofolate reductase and aldose reductase inhibitors extracted from the MDDR database, resp. This test was performed to challenge the predictive ability of the pharmacophore with two classes of inhibitors that target very different binding sites. Mol. diversity of the data sets was finally estimated by the Tanimoto approach. The results obtained provide confidence for the utility of the pharmacophore in the virtual screening of libraries and databases of compds. to discover novel PfDHFR inhibitors.

IT **180632-28-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(QSAR of Plasmodium falciparum dihydrofolate reductase inhibitors using pharmacophore generation approach)

RN 180632-28-4 CAPLUS

CN 1(2H)-Quinazolineacetic acid, 3-[[4-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethenyl]phenyl]methyl]-3,4-dihydro-2,4-dioxo- (9CI) (CA INDEX NAME)



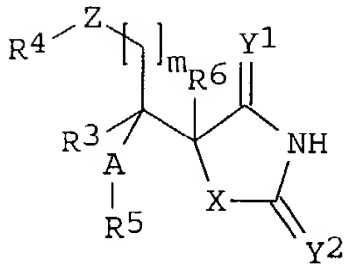
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:736238 CAPLUS
DN 137:247697
TI Preparation of 5-substituted imidazolidine-2,4-diones as metalloproteinase inhibitors
IN Lepistoe, Matti; Munck Af Rosenschoeld, Magnus
PA Astrazeneca AB, Swed.
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

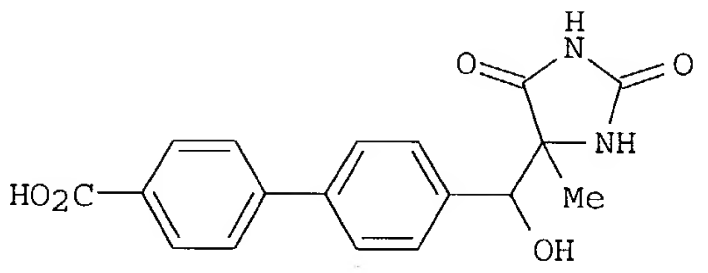
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

compounds in spec

PI	WO 2002074752	A1	20020926	WO 2002-SE479	20020313
	WO 2002074752	C1	20040422		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1370538	A1	20031217	EP 2002-704038	20020313
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	EE 200300452	A	20040216	EE 2003-452	20020313
	BR 2002008062	A	20040302	BR 2002-8062	20020313
	JP 2004527512	T2	20040909	JP 2002-573761	20020313
	NO 2003004027	A	20031105	NO 2003-4027	20030911
	US 2004110809	A1	20040610	US 2004-471499	20040112
PRAI	SE 2001-903	A	20010315		
	WO 2002-SE479	W	20020313		
OS	MARPAT 137:247697				
GI					



I



II

AB The title compds. [I; X = NR1, O, S; Y1, Y2 = O, S; Z = NR2, O, S; m = 0-1; A = a bond, alkyl, alkenyl, haloalkyl, heteroalkyl; R1, R2 = H, alkyl, haloalkyl; R3, R6 = H, halo, alkyl, etc.; R4 = H, alkyl, hydroxyalkyl, etc.; R5 = bicyclic or tricyclic group selected from (un)substituted cycloalkyl, aryl, heterocycloalkyl or heteroaryl], useful as metalloproteinase inhibitors, especially as inhibitors of MMP12, were prepared

Thus, reacting 4-carboxyphenylboronic acid with 5-[hydroxy(4-iodophenyl)methyl]imidazolidine-2,4-dione (preparation given) in the presence of NaHCO3 and Pd(OAc)2 in Me2CO and H2O afforded 34% II.

IT **459817-23-3P**

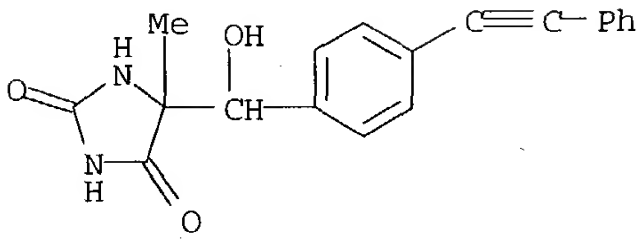
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of imidazolidine-2,4-diones as metalloproteinase inhibitors)

RN 459817-23-3 CAPLUS

CN 2,4-Imidazolidinedione, 5-[hydroxy[4-(phenylethynyl)phenyl]methyl]-5-methyl- (9CI) (CA INDEX NAME)

compounds in spec



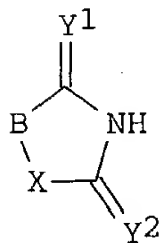
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:736236 CAPLUS
DN 137:247696
TI Preparation of 5-substituted imidazolidine-2,4-diones as metalloproteinase inhibitors
IN Eriksson, Anders; Lepistoe, Matti; Lundkvist, Michael; Munck Af Rosenschoeld, Magnus; Zlatoidsky, Pavol
PA Astrazeneca AB, Swed.
SO PCT Int. Appl., 300 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

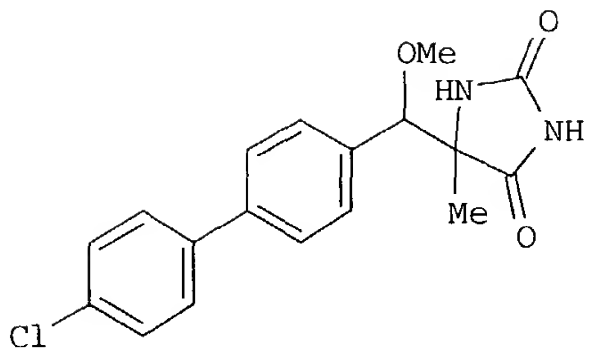
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002074750	A1	20020926	WO 2002-SE475	20020313
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EE 200300439	A	20031215	EE 2003-439	20020313
	EP 1370536	A1	20031217	EP 2002-704034	20020313
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2002008105	A	20040309	BR 2002-8105	20020313
	JP 2004527511	T2	20040909	JP 2002-573759	20020313
	NO 2003004025	A	20031113	NO 2003-4025	20030911
	US 2004147573	A1	20040729	US 2003-471808	20030912
PRAI	SE 2001-902	A	20010315		
	SE 2001-903	A	20010315		
	WO 2002-SE475	W	20020313		

OS MARPAT 137:247696
GI

compounds in spec



I



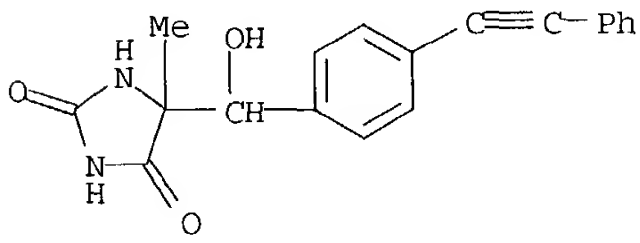
II

AB The title compds. [I; X = NR1, O, S; B = C, CH, and is a point of attachment of one or more other functional groups or side chains; Y1, Y2 = O, S; R1 = H, alkyl, haloalkyl], useful in the treatment of a disease or condition mediated by one or more metalloproteinase enzymes (no biol. data), were prepared E.g., a 4-step synthesis of II, starting with 4-(4-chlorophenyl)benzaldehyde, was given.

IT **459817-23-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 5-substituted imidazolidine-2,4-diones as metalloproteinase inhibitors)

RN 459817-23-3 CAPLUS

CN 2,4-Imidazolidinedione, 5-[hydroxy[4-(phenylethynyl)phenyl]methyl]-5-methyl- (9CI) (CA INDEX NAME)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:325919 CAPLUS
DN 130:352284
TI Preparation of 5-benzylidenethiazolidine-2,4-dione and 10-[4-[(2,4-dioxothiazolidin-5-ylidene)methyl]phenyl]-5H-dibenzo[b,e][1,4]diazepine derivatives as retinoid receptor agonists
IN Kagechika, Hiroyuki; Hashimoto, Yuichi; Itai, Akiko
PA Institute of Medicinal Molecular Design, Inc., Japan
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9924415	A1	19990520	WO 1998-JP5091	19981112

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

compounds in spec

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	CA 2309331	AA	19990520	CA 1998-2309331	19981112
	AU 9910525	A1	19990531	AU 1999-10525	19981112
	EP 1048659	A1	20001102	EP 1998-953024	19981112
	R: CH, DE, FR, GB, IT, LI				
PRAI	JP 1997-310835	A	19971112		
	WO 1998-JP5091	W	19981112		

OS MARPAT 130:352284

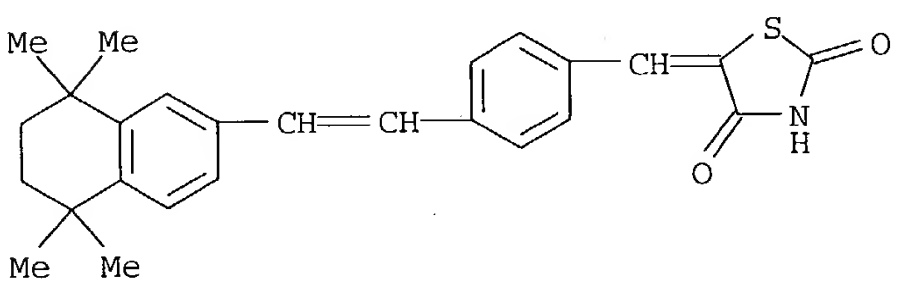
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. (I; R1-R5 = H or lower alkyl or adjacent 2 groups of R1-R5 form together with the carbon atoms of the Ph ring to from 5- to 6-membered ring optionally 1 or ≥2 alkyl groups; X = CR6:CH, CH:CR7, NR8CO, CONR9, C(:CHR10), CO, or NR11; R6-R11 = H lower alkyl) and (II; R21-R24 = H or lower alkyl or adjacent 2 groups of R1-R5 form together with the carbon atoms of the Ph ring to from 5- to 6-membered ring optionally 1 or ≥2 alkyl groups; R25 = H, lower alkyl), which are retinoid receptor agonists having retinoic effects or regulatory effects of increasing or suppressing retinoid actions, are prepared These compds. are useful for the prevention and/or treatment of cancers, diabetes, arteriosclerosis, bone diseases, rheumatism, and autoimmune diseases. Thus, 4-[1-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-7-yl)vinyl]benzaldehyde was condensed with 2,4-thiazolidinedione in the presence of piperidine and AcOH in toluene under reflux at 120° to give the title compound (III). III in vitro promoted the differentiation of HL-60 cell to granulocyte by 2.8, 6.4, and 89% at 10-8, 10-7 and 10-6 M, resp., and 76, and 84, and 92% in the copresence of 3+10-9 M Am80, resp.

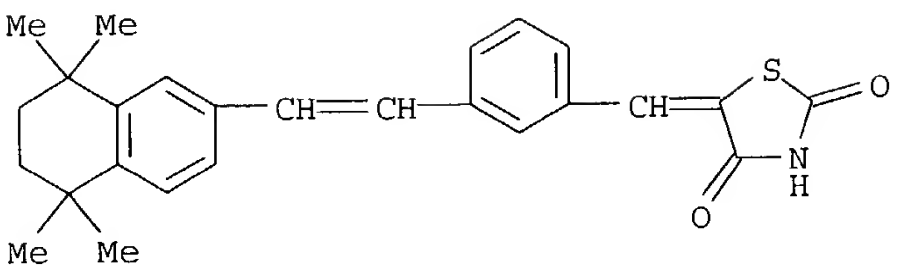
IT **224629-94-1P 224629-95-2P 224629-96-3P**
224629-97-4P 224630-07-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzylidenethiazolidinedione and [[(dioxothiazolidinylidene)methyl]phenyl]-5H-dibenzo[b,e][1,4]diazepine derivs. as retinoid receptor agonists as preventives and therapeutics)

RN 224629-94-1 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)ethenyl]phenyl]methylene]- (9CI) (CA INDEX NAME)

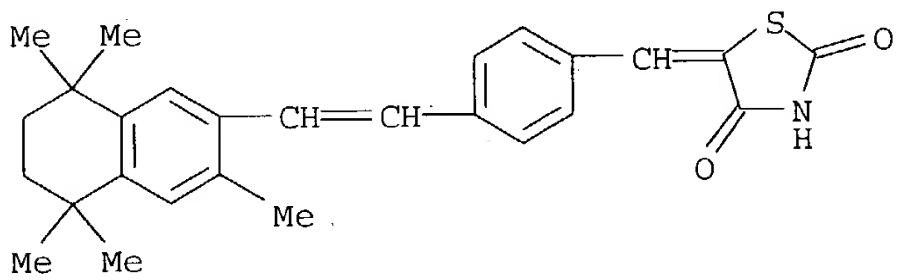


RN 224629-95-2 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[3-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)ethenyl]phenyl]methylene]- (9CI) (CA INDEX NAME)

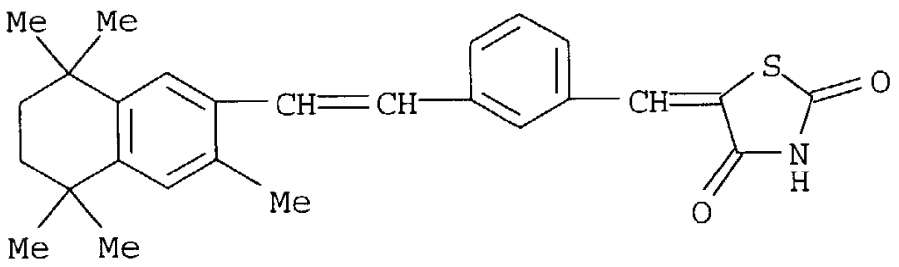
compounds in spec



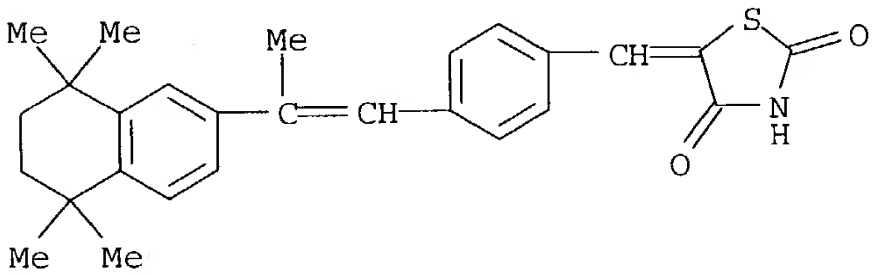
RN 224629-96-3 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)ethenyl]phenyl]methylene]- (9CI) (CA INDEX NAME)



RN 224629-97-4 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[3-[2-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)ethenyl]phenyl]methylene]- (9CI) (CA INDEX NAME)



RN 224630-07-3 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-1-propenyl]phenyl]methylene]- (9CI) (CA INDEX NAME)



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:537366 CAPLUS
DN 125:195674
TI Preparation of 2,4-dioxo-1,2,3,4-tetrahydroquinazoline derivatives having blood sugar-lowering and aldose reductase-inhibiting activity
IN Myaoka, Shozo; Sato, Hiroko; Matsushima, Hiroaki; Sugizaki, Myoshi

compounds in spec

PA Terumo Corp, Japan
SO Jpn. Kokai Tokkyo Koho, 33 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08143566	A2	19960604	JP 1994-291053	19941125
PRAI	JP 1994-291053		19941125		

OS MARPAT 125:195674
GI

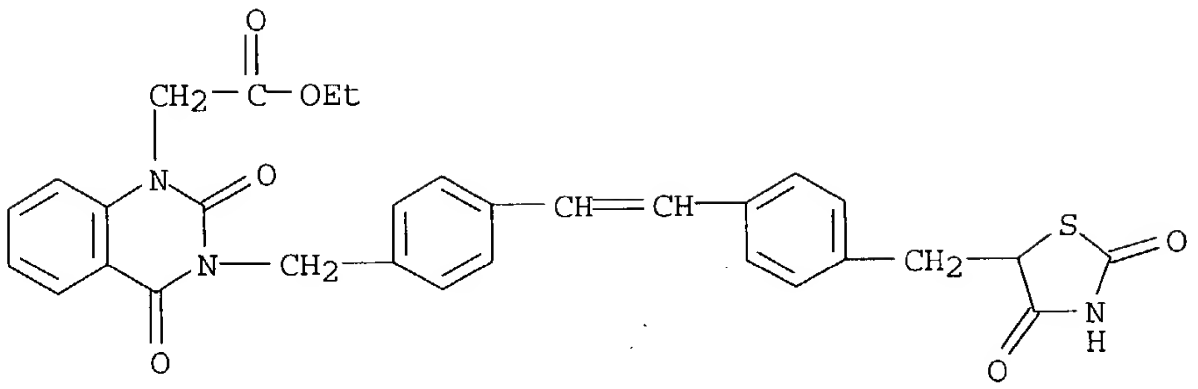
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R3, R4 = H, halo, lower alkyl, lower alkoxy, haloalkyl; R1, R2 = R5-CO2R6, CH2C6H4-A-T, (CH2)m-B-T; wherein R5 = C1-3 alkylene; R6 = H, C1-8 alkyl; A = CH2, 1,2-, 1,3-, or 1,4-NHSO2C6H4CH2, -CH2CH2C6H4CH2, or -CH:CHC6H4CH2; T = heterocyclyl having weakly acidic H; m = 1-7; B = NHSO2-C6H4-CH2], which are useful for the treatment of diabetes complications such as cataract, retinopathy, or nerve or kidney disorders, are prepared Thus, Et 2,4-dioxo-2H-3,1-benzoxazine-1(4H)-acetate, 4-nitrobenzyl amine hydrochloride, and Et3N were suspended in toluene and stirred at 100° for 2.5 h to give Et [2-[N-(4-nitrobenzyl)carbamoyl]phenylamino]acetate, which was cyclocondensed with 1,1'-carbonyldiimidazole at 130° for 2 h to I (R1 = 4-nitrobenzyl, R2 = CH2CO2Et, R3 = R4 = H), diazotized with NaNO2 in HBr/aqueous acetone at 5°, and coupled with Et acrylate in the presence of Cu2O at 30° to give I (R1 = Q, R2 = CH2CO2Et, R3 = R4 = H). The latter compound was cyclocondensed with thiourea in the presence of AcONa in ethanol under reflux for 6 h to I (R1 = Q1, wherein Z = NH, R2 = CH2CO2Et, R3 = R4 = H), which was hydrolyzed in 2 N aqueous HCl under reflux to give I (R1 = Q1, wherein Z = O, R2 = CH2CO2Et, R3 = R4 = H) and I (R1 = Q1, wherein Z = O, R2 = CH2CO2H, R3 = R4 = H). I (R1 = Q2, R2 = CH2CO2H, R3 = 7-Cl, R4 = H) and I (R1 = Q3, R2 = CH2CO2H, R3 = R4 = H) in vitro showed IC50 of 3.34 + 10-8 and 2.13 + 10-6 M, resp., against aldose reductase, and at 100 mg/kg/day p.o. for 2 days in vivo lowered blood sugar by 13 and 36%, resp.

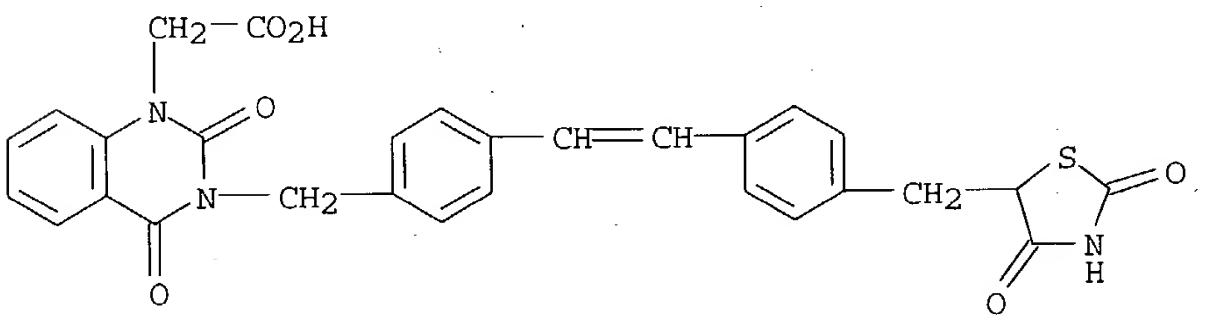
IT **180632-27-3P 180632-28-4P 180632-29-5P**
180632-30-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dioxotetrahydroquinazoline derivs. having blood sugar-lowering and aldose reductase-inhibiting activity for treating diabetes complications)

RN 180632-27-3 CAPLUS
CN 1(2H)-Quinazolineacetic acid, 3-[[4-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethenyl]phenyl]methyl]-3,4-dihydro-2,4-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

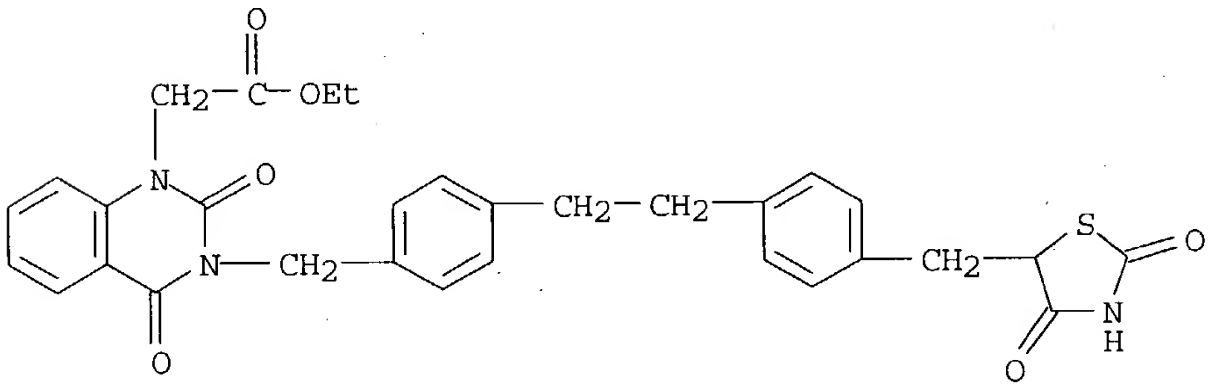
compounds in spec



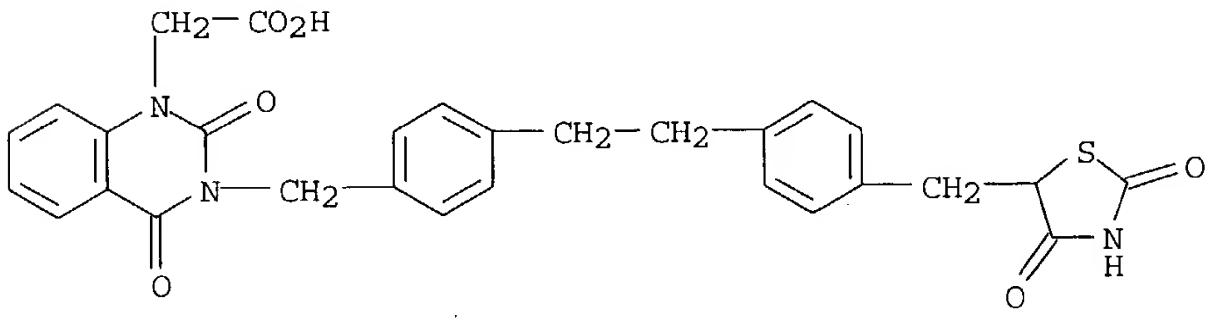
RN 180632-28-4 CAPLUS
CN 1(2H)-Quinazolineacetic acid, 3-[[4-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethenyl]phenyl]methyl]-3,4-dihydro-2,4-dioxo- (9CI) (CA INDEX NAME)



RN 180632-29-5 CAPLUS
CN 1(2H)-Quinazolineacetic acid, 3-[[4-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]phenyl]methyl]-3,4-dihydro-2,4-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

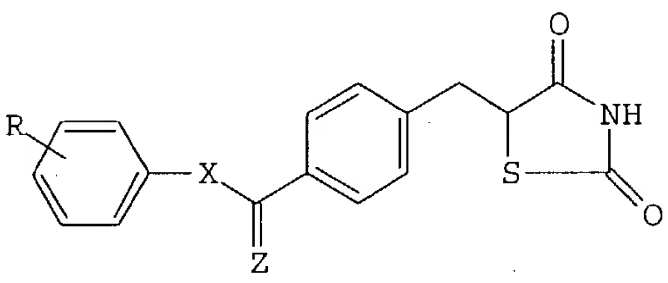


RN 180632-30-8 CAPLUS
CN 1(2H)-Quinazolineacetic acid, 3-[[4-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]phenyl]methyl]-3,4-dihydro-2,4-dioxo- (9CI) (CA INDEX NAME)

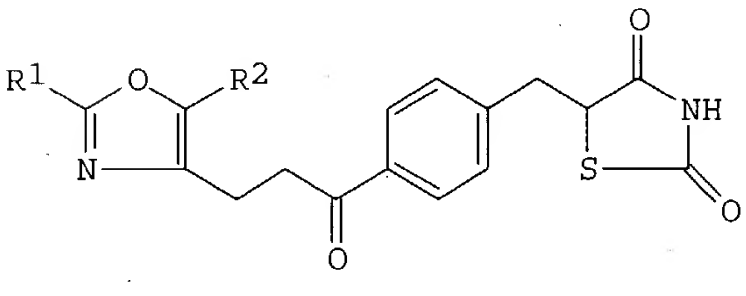


compounds in spec

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:255519 CAPLUS
DN 116:255519
TI Novel thiazolidine-2,4-diones as potent euglycemic agents.
AU Hulin, Bernard; Clark, David A.; Goldstein, Steven W.; McDermott, Ruth E.; Dambek, Paul J.; Kappeler, Werner H.; Lamphere, Charles H.; Lewis, Diana M.; Rizzi, James P.
CS Pfizer Inc., Groton, CT, 06340, USA
SO Journal of Medicinal Chemistry (1992), 35(10), 1853-64
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



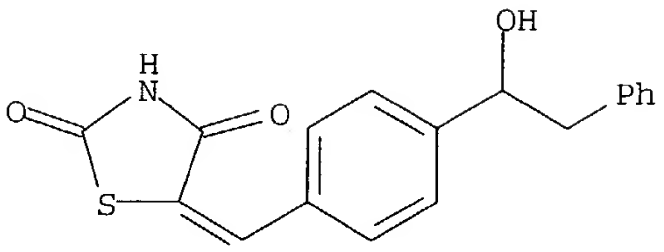
I



II

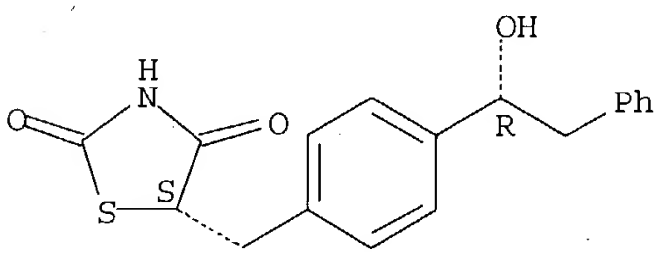
AB A new series of thiazolidine-2,4-diones I [R = H, Z = O, X = (CH2)n, (n = 1, 2, 3), OCH2, CH:CH; R = 4-PhCH2O, 4-Ph, 2-MeO, 4-MeO, Z = O, X = CH2CH2; R = H, Z = H2 or H,OH, X = CH2CH2; R = 4-PhCH2O, 2-MeO, 2-Cl, 2-CF3, 2-PhCH2, 3-Cl, 4-Br, 4-EtO2C, 4-Ph, 2-HO, 2-Me, 4-MeOCH2, 4-MeO, 4-Me2N, Z = O, X = CH:CH] was obtained by replacing the ether function of englitazone with various functional groups, i.e., a ketone, alc., or olefin moiety. These compds. lower blood glucose levels in the genetically obese and insulin-resistant ob/ob mouse. Appending an oxazole-based group at the terminus of the chain provided highly potent compds., e.g. II [R1 = Ph, 4-MeC6H4, R2 = Me, H; R1 = 4-MeOC6H4, 4-CF3C6H4, 4-HOC6H4, 3,5,4-Me2(MeO)C6H2, 3,5,4-Me2(HO)C6H2, 2-furyl, 2-(5-methylfuryl), 2-HSC6H4, 2-naphthyl, R2 = Me].
IT **141200-90-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with thiazolidinedione)
RN 141200-90-0 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-(1-hydroxy-2-phenylethyl)phenyl]methylene]-(9CI) (CA INDEX NAME)

compounds in spec



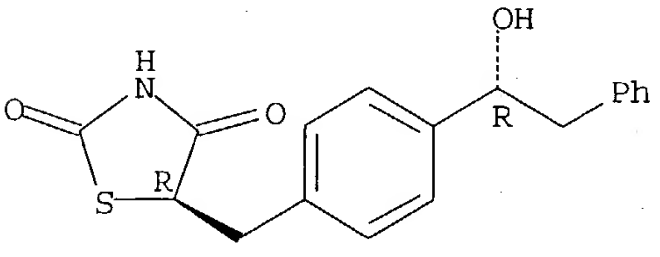
IT **141200-92-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and conjugate redn of, in preparation of euglycemics)
RN 141200-92-2 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-(1-hydroxy-2-phenylethyl)phenyl]methyl]-, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



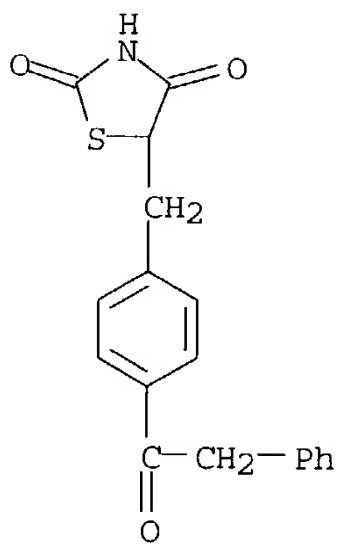
IT **141200-91-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and conjugate reduction of, in preparation of euglycemics)
RN 141200-91-1 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-(1-hydroxy-2-phenylethyl)phenyl]methyl]-, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **141199-89-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and euglycemic activity of)
RN 141199-89-5 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-(phenylacetyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

compounds in spec



=> d bib 1-3

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:325919 CAPLUS
DN 130:352284
TI Preparation of 5-benzylidenethiazolidine-2,4-dione and 10-[4-[(2,4-dioxothiazolidin-5-ylidene)methyl]phenyl]-5H-dibenzo[b,e][1,4]diazepine derivatives as retinoid receptor agonists
IN Kagechika, Hiroyuki; Hashimoto, Yuichi; Itai, Akiko
PA Institute of Medicinal Molecular Design, Inc., Japan
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9924415	A1	19990520	WO 1998-JP5091	19981112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2309331	AA	19990520	CA 1998-2309331	19981112
AU 9910525	A1	19990531	AU 1999-10525	19981112
EP 1048659	A1	20001102	EP 1998-953024	19981112
R: CH, DE, FR, GB, IT, LI				
PRAI JP 1997-310835	A	19971112		
WO 1998-JP5091	W	19981112		

OS MARPAT 130:352284
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:537366 CAPLUS
DN 125:195674
TI Preparation of 2,4-dioxo-1,2,3,4-tetrahydroquinazoline derivatives having blood sugar-lowering and aldose reductase-inhibiting activity
IN Myaoka, Shozo; Sato, Hiroko; Matsushima, Hiroaki; Sugizaki, Myoshi
PA Terumo Corp, Japan

compounds in spec

SO Jpn. Kokai Tokkyo Koho, 33 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 08143566	A2	19960604	JP 1994-291053	19941125
PRAI JP 1994-291053		19941125		

OS MARPAT 125:195674

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:255519 CAPLUS
DN 116:255519
TI Novel thiazolidine-2,4-diones as potent euglycemic agents.
AU Hulin, Bernard; Clark, David A.; Goldstein, Steven W.; McDermott, Ruth E.; Dambek, Paul J.; Kappeler, Werner H.; Lamphere, Charles H.; Lewis, Diana M.; Rizzi, James P.
CS Pfizer Inc., Groton, CT, 06340, USA
SO Journal of Medicinal Chemistry (1992), 35(10), 1853-64
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English

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